



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Brian R. Murphy, et al.

Application No.: 09/083,793

Filed: May 22, 1998

Examiner: M. Mosher

Group Art Unit: 1648

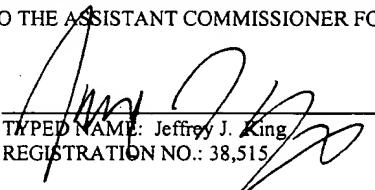
DECLARATION OF BRIAN R. MURPHY

UNDER 37 CFR 1.132

For: PRODUCTION OF ATTENUATED  
PARAINFLUENZA VIRUS FROM  
CLONED NUCLEOTIDE SEQUENCES

DATE OF DEPOSIT: August 26, 2002

I HEREBY CERTIFY THAT THIS PAPER IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE AS FIRST CLASS MAIL, POSTAGE PREPAID ON THE DATE INDICATED ABOVE AND IS ADDRESSED TO THE ASSISTANT COMMISSIONER FOR PATENTS, WASHINGTON, DC 20231.

  
TYPED NAME: Jeffrey J. King  
REGISTRATION NO.: 38,515

Assistant Commissioner for Patents  
Washington, D.C. 20231

Dear Sir:

I, Brian R. Murphy, M.D., declare as follows:

1. I am presently employed as co-head of the Laboratory of Infectious Diseases within the National Institute for Allergies and Infectious Diseases (NIAID) of the National Institutes of Health (NIH). I have been directly involved with this laboratory for over thirty years, beginning with my initial post as a research physician studying respiratory viral diseases in 1970. My Curriculum Vitae and Bibliography of publications are attached.

2. As current head of the respiratory virus section within NIAID, I oversee the research activities of more than 25 research professionals within the section. For approximately 17 years, our efforts have focused on vaccine development for parainfluenza virus (PIV).

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3. I have read and fully understand the specification and claims of the above-identified patent application, on which I am a co-inventor.

4. I have reviewed and carefully considered the substantive Office Actions (identified as Papers No. 10, 17, and 22) presented in the above-identified application.

5. I have carefully reviewed the Belshe et al. reference (U.S. Patent No. 5,869,036) cited in the above-noted Office Actions.

6. The facts presented and discussed below are directed to two principal issues raised in the current Office Action (Paper No. 22): (1) Does the Belshe et al. specification cited by the Office teach or suggest the subject matter as recited in the rejected claims of the current application? And (2) Does the current application teach how to make and use the subject matter set forth in the pending claims without undue experimentation considering the level of predictability in the art?

7. Considering all of the facts presented in the record, as discussed herein below, I conclude that the Belshe et al. patent (alternatively, the '036 patent) does not provide sufficient description and guidance to permit a person of ordinary skill in the art (at either the time the Belshe et al. patent or the current application was filed) to recover a recombinant parainfluenza virus (PIV) from cDNA. On the contrary, the Belshe et al. specification only hypothetically discusses the possibility of recovering a recombinant PIV from cDNA. No such cDNA nor recombinant PIV is actually described in structural terms that would qualify as a "written description" of such materials, and it is apparent that no "working example" of a cDNA encoding a recombinant PIV, nor of an actual recombinant PIV, is provided by the Belshe et al. disclosure. Additionally, considering the level of predictability in the art prior to the discoveries presented in the instant application, the teachings of Belshe et al. would not have been considered to provide an "enabling" disclosure of the presently claimed invention. That is to say, Belshe et al. offer such limited direction and guidance that, even when supplemented by available knowledge in the art at the time the instant application was filed, the skilled artisan would not have considered the public to be placed "in possession of" a recombinant PIV produced from cDNA. This conclusion, and the related conclusions below, relate to the fundamental technology of the present invention, i.e., successful recovery of a viable, self-replicating, recombinant PIV from cDNA. It is even more clear that certain detailed aspects of the invention, e.g., involving identification and manipulation of attenuating mutations and their introduction, singly and in combination, into a recombinant PIV, and

successful recovery of chimeric PIVs, and attenuated chimeric PIVs, are neither disclosed nor suggested by Belshe et al.

8. Considering the specific issue of "obviousness" raised by the Office, I conclude that the limited teachings of Belshe et al. fail to provide a practical suggestion or motivation that would have led the skilled artisan to undertake production of a recombinant PIV from cDNA with a "reasonable expectation of success". Considering the poorly developed state of knowledge and high degree of unpredictability in the art, among other technical challenges discussed below, to achieve this goal without the benefit of the instant disclosure would have been viewed by the skilled artisan as requiring such extensive and uncertain experimentation that would have been characterized as "undue" experimentation--unattended by a "reasonable expectation of success". The same facts, set forth below, that support this conclusion also point to a conclusion that the instant disclosure provides "unexpected results" in the successful production of a recombinant PIV from cDNA. Concerning more detailed aspects of the invention, the results provided by the instant disclosure allow production of singly and multiply attenuated, recombinant PIVs, chimeric PIVs, and attenuated chimeric PIVs, that are sufficiently infectious in a mammalian host to generate a desired immune response yet are suitably attenuated for selection and development as PIV vaccine candidates. That these novel results were achieved within the instant invention was even more surprising that the basic recovery of recombinant PIV, based on the limited teachings of Belshe et al. combined with general knowledge in the art at the time of the invention.

9. With respect to the issue of enablement newly raised by the Office, I conclude that the present disclosure provides sufficient description and guidance to enable the skilled artisan to practice the invention in a manner fully commensurate with the scope of the claims presented for review. In particular, the application details materials and methods and provides extensive working examples that teach how to make and use recombinant PIVs from cDNA--in a manner that correlates reasonably with the full breadth of the claims. Numerous recombinant PIVs having representative modifications, such as a chimeric construction and/or single and multiple attenuating mutations, are provided. These examples constitute a representative assemblage of species commensurate with the full scope of the claims. These representative species are shown by detailed, *in vitro* and *in vivo* working examples to have the desired characteristics for use as vaccine candidates. As stated previously in the record, prior to the instant invention such materials and methods would have been considered highly unpredictable. This unpredictability does not, however, translate to the presently claimed invention that

was achieved through an exhaustive, successful research campaign culminating in the instant disclosure. Following this detailed disclosure, the artisan can now readily undertake production and selection of additional operable species within the claims, and thereby practice the invention commensurate with the full scope of the claims without "undue experimentation". This is true even though certain species that fall within the claims may be sub-optimal or even inoperable for vaccine production.

10. Turning now to the facts of record that support the foregoing conclusions, the Belshe et al. specification fails to provide a single example of a recombinant PIV recovered from a cDNA. On the contrary, the Belshe et al. reference is limited in its teachings to a purported *in vitro* complementation assay described to evaluate temperature sensitivity. This limited study is attended by fundamental flaws in its design and interpretation, as discussed below. Even if the Belshe et al. complementation assay results are accepted as reported, there is no theoretical or empirical basis to extrapolate these findings into the context of a complete, infectious virus and, most importantly, to the production of a recombinant PIV that is viable, attenuated, and immunogenic *in vivo*.

11. In contrast to the deficient teachings of Belshe et al., the instant application provides detailed working examples that detail production and employment of cDNAs to yield successful recovery of (1) recombinant wild type human parainfluenza virus type 3 (PIV3); (2) multiple recombinant PIV3s containing well defined single attenuating mutations; (3) multiple recombinant PIV3s containing more than one attenuating mutation in combination; (4) a chimeric PIV3-1 virus in which the HN and F open reading frames (ORFs) of wild type PIV3 were replaced with ORFs encoding the counterpart HN and F proteins of PIV1; and (5) viable, immunogenic derivatives of chimeric PIV3-1 having defined attenuating mutations incorporated in the chimeric virus.

12. Belshe describes a simple, *in vitro* complementation assay in which a plasmid expressing a wild type L protein in a transfected cell monolayer reportedly increased the level of replication of PIV3 cp45 from  $10^1$  (Table 1 in the Belshe patent) to  $10^{2.3}$  PFU/ml (Table 2 in the Belshe patent) at 39.5°C. Importantly, a control plasmid containing the cp45 mutations was not evaluated in this complementation assay, and thus the difference identified in the complementation assay cannot be ascribed to the sequence differences between the wild type and cp45 PIV3 L protein. In addition, the L cDNA employed by Belshe et al. was not evaluated for its effect on replication of wild type HPIV3. This is a critical control that would address the very real possibility that the modest increase in virus replication was simply due to increased expression of L protein, which is expressed at very low levels during virus infection. Thus, the increase may reflect a "dose effect" rather than true complementation

of a *ts* defect. The assay of Belshe et al. (see Table 3) is also unreliable in other crucial aspects. For example, complementation with L and P reportedly yielded 190 infectious virus particles. The further inclusion of NP reportedly yielded 2,300 plaque forming units (pfu), a 12-fold increase that, by the logic of the assay, would seem significant and would reasonably be interpreted as evidence that cp45 NP must contain one or more critical temperature sensitive or attenuation mutations. Yet, the sequence information provided in Fig. 1 of Belshe et al. indicates that cp45 NP does not contain a single mutation compared to wild type. Thus, the purported positive results in the complementation assay contain internal inconsistencies and lack the essential verification of important experimental controls. This determination would have been clear to the skilled artisan and would have detracted significantly from the motivation provided by the cited reference and the expectation of success that the artisan would have to practice the presently claimed invention as allegedly taught or suggested by Belshe et al.

13. The 20-fold increase in replication of cp45 at 39.5°C in the presence of L reported by Belshe et al. was interpreted as indicating that the mutations in the L protein of cp45 specify an attenuation phenotype. It is important, however, to place the complementation findings reported by Belshe et al. in appropriate scientific context. A typical yield of wild type HPIV3 from  $3 \times 10^6$  cells (as in the experiment of Belshe et al.) would be expected to be  $5 \times 10^8$  pfu or more, such that each cell produces more than 100 pfu. The complementation assay of Belshe with L alone yielded 330 pfu for the entire culture. This suggests that as few as 3 or 4 cells (and certainly no more than 330 cells) successfully produced virus, whereas the remaining several million failed to produce a single particle. Hence, even if the complementation is accepted as authentic, it is of such a low efficiency that its significance is highly doubtful. In any case, there are no means for extrapolating findings from such a complementation assay to infectious virus. Thus, the 20-fold increase in the replication seen in the complementation assay cannot be extrapolated to predict or understand the magnitude of the contribution of the L protein mutations to the *ts* phenotype of cp45, nor what the biological properties of a hybrid virus carrying only these mutations might be. At best, the findings are simply suggestive that the L gene mutations might contribute to some undefined portion of the temperature sensitivity of the cp45 virus. Furthermore, and most importantly, the complementation assay of Belshe relates only to the *ts* phenotype of cp45, and does not address the attenuation phenotype *in vitro* or *in vivo*. While a *ts* phenotype often is associated with attenuation, it is not possible to predict that attenuation will indeed result, nor what its magnitude might be. This is a critical deficiency, since the level of attenuation *in vivo* is essential to assess the safety of a vaccine virus. Only by actually making an infectious recombinant virus, as provided in multiple working examples in the present disclosure, can one assess

the *in vivo* attenuation of the virus to determine its usefulness as a vaccine candidate. Again, each of these deficiencies of Belshe et al. would have been clear to the skilled artisan and would have undermined the motivation and expectation of success for practicing the claimed invention following the teachings of Belshe et al.

14. Only with the aid of the present disclosure providing a successful cDNA recovery system can the phenotypic effect of any desired mutation (e.g., an attenuating mutation from PIV3 cp45) be evaluated and demonstrated. For example the instant disclosure demonstrates that a ts mutation identified in L can be segregated from complementary or interactive effects of other cp45 mutations. In this context, it is critical for evaluating the speculative teachings of Belshe et al. that at least a representative set of mutations identified and segregated into a viable recombinant vaccine candidate be verified as attenuating, and that such attenuation be balanced sufficiently to yield a protective immune response in susceptible hosts. The simple studies of Belshe et al. were limited to complementation of replication for a cp45 virus using a wild type L plasmid. These studies were only conducted *in vitro* using tissue culture cells, and were not validated by parallel studies *in vivo*. In this context, it was quite possible that recombinant viruses incorporating one or more of the three "temperature sensitive" (ts) mutations in the cp45 L gene mutations would not be attenuating (att) *in vivo*. In particular, a finding that replication of cp45 may be complemented by wild type L protein in tissue culture cells is not clearly predictive that a virus bearing one or more of these mutations would be attenuated *in vivo*. This correlative deficiency is apparent from the following considerations. As an initial point, it is known that entire classes of viruses called "temperature-dependent host range (td-hr) mutants" may be ts on one tissue but not on other tissue culture cells. These td-hr mutants are not necessarily attenuated *in vivo* (see Snyder et al., Virus Research 15:69-84, 1990 and Shimizu et al., Virology 124:35-44, 1983). As described in Snyder et al., an exemplary mutant (clone 143-1) of influenza virus was shown to be highly ts in tissue culture cells, but was not significantly attenuated *in vivo*. Additional findings by Shimizu et al. indicate that such td-hr mutants are common and are found in many different complementation groups of the influenza virus (i.e., they are present in many different genes of the virus). The Belshe et al. reference does not demonstrate whether any of the contemplated ts mutations in the L gene of cp45 belong in the td-hr class of mutations or in the other class of ts mutations whose replication is effected by the temperature present in the host animal. In view of this deficiency, the simple description of a complementation phenotype for a group of multiple, unsegregated mutations in a complete gene *in vitro* does not serve as a reliable indicator of attenuation *in vivo*. As detailed herein, the instant disclosure provides the basic tools, along with fully detailed description and guidance, to resolve these deficiencies

and enable the skilled artisan to practice the invention throughout the scope of the claims presented for review.

15. I further note that the sequence of the cp45 L gene claimed by Belshe was taken directly from published work by others in our laboratory in 1993 (Stokes et al, 1993 Virus Research 30:43). Thus, the mutations in L evaluated by Belshe were already described in the literature and were considered possible attenuating mutations. In this context, the Belshe et al. disclosure provided little new information on the nature of the genetic determinants of the ts phenotype of cp45--only following previous suggestions that one or more mutations in L might specify some portion of the ts phenotype in cp45. In contrast, by describing successful recovery of recombinant PIV from cDNA, and by further incorporating individual and combinatorial mutations from cp45 (from several genes as well as from extragenic portions of the genome) in recombinant PIVs, the instant disclosure dissects and maps out the specific contributions of the individual lesions in cp45 to the attenuation phenotype. Following introduction of these various, representative mutations, singly and in combination, into recombinant PIVs, the ability to achieve an attenuation phenotype using various manipulations, and to fine tune the attenuation phenotype to achieve useful vaccine strains, was established using widely accepted *in vivo* models for attenuation and immunogenic activity in humans.

16. The sequences of the PIV3 cp45 virus reported by Belshe et al. rely completely on the published sequences of others (Stokes et al, 1993 Virus Research 30:43), as noted above, and it is important to consider that those sequences were subsequently found to contain errors that were corrected by the present disclosure. The complete, correct sequence of cp45 is presented in current specification. This information, combined with the first successful attempt to generate recombinant PIVs containing various combinations of these mutations, defined the major attenuating mutations in PIV3 cp45 to be in the genes encoding not only the L protein, but also the C and F proteins. The present work also provided the first analyses of virus replication, immunogenicity and protective efficacy for these single and combinatorial mutants in accepted models for PIV infection and vaccine development. Examination of Figure 1 of the Belshe et al. patent fails to identify the mutation in C. The Figure only reiterates the incomplete sequence information and analysis previously reported by Stokes et al. From Belshe et al., one would not know that the F or C mutations present in cp45 were attenuating mutations, and that these mutations are useful in cDNA-derived recombinant vaccine viruses. The materials and methods described in the instant disclosure not only identified the attenuating mutations present in cp45, but provided a general method that later proved useful in identifying other attenuating mutations present in

heterologous viruses such as a mutation designated 456 from the respiratory syncytial virus (RSV) L protein, a mutation designated 170 from the Sendai virus C protein, and a mutation designated 1711 mutation from the L protein of bovine PIV3 (BPIV3), for incorporation into recombinant PIVs of the invention (data will be provided if requested by the Office).

17. As noted above, recovery of a recombinant virus from cDNA was not accomplished by Belshe et al. Nonetheless, the reference speculates even further concerning the prospect of hybrid (chimeric) recombinant vaccine viruses (Example 7), and such recombinant viruses are referred to in multiple claims of Belshe et al. However, the reference clearly fails to describe or enable any chimeric cDNA constructs or methods for recovering chimeric viruses from cDNA, nor to characterize any chimeric viruses *in vitro* or *in vivo* for identification of useful vaccine candidates. Thus, although the principal disclosure of Belshe et al. purports to render construction of chimeric PIV and other "hybrid" viruses possible, the reference neither describes, teaches nor suggests the presently claimed subject matter. On the contrary, no specific guidance is provided to enable any kind of cDNA recovery of PIV, much less recovery of a viable, attenuated and infectious chimeric PIV as provided by the instant disclosure. The speculative teachings of Belshe et al. would not have been accepted by the skilled artisan as providing a clear teaching or practical motivation to achieve the presently claimed invention. This conclusion is underscored by the vast diversity of viral "targets" contemplated by Belshe et al. for constructing "hybrid" viruses, as indicated by the following passage:

Hence, in addition to related enveloped, negative-sense, single-stranded RNA viruses such as human parainfluenza virus type 1 (HPIV-1), human parainfluenza virus type 2 (HPIV-2), respiratory syncytial virus (RSV), human influenza virus type A, human influenza virus type B, and measles viruses, target viruses would also include other enveloped viruses, such as paramyxoviruses, orthomyxoviruses, retroviruses (e.g. human immunodeficiency viruses HIV-GP120 and HIV-GP41), arenaviruses, coronaviruses, bunyaviruses, rhabdoviruses, togaviruses, herpesviruses, poxviruses and hepadnaviruses. Preferable target viruses include enveloped viruses which reproduce in the cytoplasm. The target virus of the present invention may be specific to humans, specific to animals or common to both animals and humans. Bovine RSV and cattle HPIV-3 (shipping fever virus) are typical animal viruses included within the scope of the present invention. [Col. 8, lines 42-58, underscore added.]

In contrast to these broad, prophetic and overreaching statements, the present specification provides detailed description and guidance, as well as a fully representative assemblage of working examples

(e.g., various attenuated PIV3-1 chimeric vaccine candidates) that is fully commensurate with the scope of claims presented for review.

18. The differences between the present disclosure and the Belshe et al. reference relating to the description of a system to recover infectious replicating viruses from cDNA for selection as vaccine candidates are outlined in Tables 1–3 below, and are briefly addressed in the following paragraphs.

**Table 1 – Comparison of PIV3 and of chimeric PIV3 cDNA constructs used to rescue viable virus**

Requirements for successful rescue of recombinant PIV3 and of chimeric PIV3 virus	Described in Murphy 09/083,793	Described in Belshe 5,869,036
Characteristics of PIV3 cDNA  a- Viable (free of errors) PIV3 sequence  b- specified length ("rule of six"[described below])  c- sequence that specifies a virus capable of being recovered and capable of efficient replication in cell culture and animals  d- Structure of the expression plasmid into which PIV3 sequences are placed, strategy for producing correct 3' and 5' ends, and conditions for stable propagation in bacteria	Complete description of viable sequence and construction of cDNAs and expression plasmids from which PIV3 was recovered (confirming authenticity of sequence and effectiveness of recovery conditions); efficient replication of recovered virus in vitro and in vivo	Sequence of cDNA construct for PIV3 not provided; construction not described. Recovery of recombinant virus not described.
Characteristics of chimeric virus with insert  a- viable sequence  b- specified length and strict adherence to the rule of six  c- sequence at chimeric junctions	Complete description of DNAs and protocol; demonstration of successful recovery indicating authenticity of construct; confirmation of virus characteristics	Sequences of insert not provided; sequences of backbone not provided; junctions not specified, construction not described, recombinant virus not recovered

provided		
d- replication competent vector backbone, wild type nature of insert sequence		
e- construction of cDNA and expression plasmid		
Characteristics of full-length cDNA for attenuated PIV3 or chimeric virus  a- viable sequence  b- specified length ("rule of six")  c- sequence at chimeric junctions  d- construction of cDNA and expression plasmid  e- replication competence of virus derived from cDNA	Complete description, demonstration of recovery and analysis of virus	Sequence of a full length cDNA from which attenuated PIV3 or attenuated virus not provided; construction not described, recombinant virus not recovered

19. Referring to Table 1, it is noted that the Belshe et al. application fails to provide an accurate sequence of a wild type PIV virus. This is a critical deficiency for describing and enabling the instantly claimed invention. Notably, PIV lacks a proof-reading polymerase and is known to have a high error rate. During cDNA cloning this high error rate is reflected in a relatively large number of sequence differences among clones, which are heightened by additional errors introduced during RT, PCR, and propagation in bacteria. A single point mutation in the 15.4 kb sequence can be sufficient to preclude recovery, and the identification and correction of potential errors presents a formidable challenge. The sequences described in Stoke's et al. and incorporated by Belshe et al. were later modified by the instant disclosure to correct errors, and the ultimate recovery of infectious virus verified that the presently described sequence is "viable". Thus, Belshe et al. rely on the previously reported sequence by Stokes et al., and there was no evidence at the time that this sequence, shown in the present

disclosure to be inaccurate, could have yielded a viable virus. Even if this untested, incorrect sequence were employed successful to obtain a recombinant virus, it was nonetheless unpredictable whether the sequence would specify a replication competent phenotype, i.e., a level of replication compatible with immunogenicity *in vivo*. Thus, Belshe et al. would not have been considered by the skilled artisan to enable recovery of a recombinant PIV3 nor a chimeric vaccine virus, since there was insufficient evidence that the reported sequence would yield these required results. Only the instant disclosure provides an authentic sequence of the full length PIV3 and its contiguous sequences in a plasmid with correct T7 promoter elements, T7 terminators, and hepatitis delta ribozyme. It is noteworthy that during the nearly seven years after the filing date of Belshe et al., Belshe and coworkers have apparently failed to recover any PIV from cDNA. In contrast, the instant disclosure provides a large, fully representative panel of recombinant viruses, including singly and multiply attenuated viruses and chimeric viruses. Among these recombinant viruses, PIV3 and PIV1 viruses and chimeric "vectors" have been constructed and demonstrated to be suitably attenuated and immunogenic to yield protection against PIV1, PIV2, and PIV3. Following these detailed teachings, our lab has progressed into clinical studies for PIV vaccine candidates recovered from cDNAs.

20. In further reference to Table 1, Belshe et al. fails to describe or enable any specific sequence for an "insert" to yield a chimeric virus that would be compatible for efficient replication in a PIV3 backbone. Instead, Belshe et al. simply reference viral proteins, but do not specify any specific sequence of any insert, nor an insert length (columns 17–18). Since there were many sequence errors existing in the literature, it would not have been possible to determine whether the chimeric viruses prophetically reported by Belshe et al. would be viable, or, if viable, would possess a replication competent phenotype, i.e., a level of replication compatible with immunogenicity *in vivo*. In contrast, the PIV1 sequences used in the construction of chimeric cDNAs of the present invention to generate a PIV3-1 virus were obtained from a wild type PIV1 of known virulence for humans and, following insertion into the PIV3 backbone, yielded a chimeric virus with a verified wild type phenotype. The genes that encode the proteins alluded to by Belshe et al. include gene start sequences, a 5' non-coding region, coding region, 3' non-coding region, and gene-end sequence. The exact junctions of the sequences for the inserts referred to by Belshe et al. were not described and therefore one would not have known from the Belshe et al. description whether to include any of the extra-coding sequences or not. For example, the genes from any given virus contain transcription signals that differ from those of another virus, yet it is essential that the "transferred" gene be faithfully expressed in the new, heterologous viral backbone. This critical issue is not even addressed in the Belshe et al. specification.

In contrast, the instant disclosure provides exemplary descriptions of an insert, backbone, transcription signals and junctions to yield viable chimeric PIVs that are useful vaccine candidates.

21. Yet another critical deficiency of Belshe et al. that is resolved by the present disclosure relates to the length of the viral genome for production of recombinant PIVs. The length of the PIV genomes need to be an even multiple of six in order to recover authentic copies of virus containing the exact sequence in the cDNA. This "rule of six" reflects the association of each NP monomer with six nucleotides. If the genome does not conform to the rule of six, mutant viruses are recovered that have random mutations that correct the length. This factor adds a major aspect of uncertainty to the teachings of the Belshe et al. reference, which fails to appreciate the significance of the rule of six and the errors that would arise by failure to properly construct cDNAs in accordance with this requirement. In the instant disclosure, the exact lengths of a full length cDNA for PIV3 (number of nucleotides = 15462) and for PIV3-1 (number of nucleotides = 15516) are provided. This description in turn depended on the actual, successful recovery of recombinant PIVs and subsequent analysis and verification of the fidelity of the viral sequence and phenotype.

**Table 2– Comparison of system used to recover virus from recombinant PIV3 or chimeric cDNA constructs**

Requirements for successful rescue of recombinant chimeric PIV3 virus	Described in Murphy	Described in Belshe
Description of method used to recover infectious virus from chimeric cDNA including cell type, quantities of the full length genomic cDNA and support plasmids cDNA, source of T7 polymerase, compatibility of vaccinia virus expressing T7 with the virus to be recovered, method of isolating the recovered PIV	Exact transfection reaction described that yielded recombinant chimeric virus	Infectious virus not recovered –a method is described in very general terms and was not demonstrated to yield recombinant virus

22. In Table 1, above, the requirements for sequences of a full-length cDNA to successfully recover infectious, recombinant PIV are described. The specific methods used to recover infectious virus also need to be described to enable production of recombinant viruses from cDNAs. Systems to recover negative stranded RNA viruses such as PIV from cDNA are complicated and require a suitable cell capable of both successful transfection by plasmids and replication of the rescued virus. It should be noted that the recovery of infectious recombinant negative stranded RNA viruses is generally quite inefficient, such that out of 1,000,000 transfected cells, 10 or fewer cells actually produce virus (of course, once a recombinant virus is produced, it can then be propagated efficiently and evaluated like a biologically-derived virus). Particularly for a human pathogen such as PIV3, which does not grow rapidly *in vitro*, it is a formidable challenge to successfully produce and recover recombinant virus from cDNA. Our studies confirmed that the precise amount of the viral cDNA and support plasmid DNA was critical for initial recovery of recombinant PIV, and this factor was not appreciated by Belshe et al., who failed to even initiate a recovery system. As another example of inadequate guidance, Belshe et al. describe prophetically the use of cDNA expressing a genome sense RNA to recover virus (column 10, line 35). It is now known, however, that for technical reasons the recovery of virus from genome-sense RNA is relatively inefficient at best, and often unsuccessful. An optimal strategy employs a cDNA expressing a positive sense copy of the genome (called an antigenome). This guidance is clearly provided in present disclosure.

23. To enable production of a recombinant PIV from cDNA, a description of a system to promote expression of viral proteins from support plasmids and from a full-length cDNA that can form a functional transcriptase/replicase/genome complex is needed. A full description of this system is required, and notably lacking in the disclosure of Belshe et al. For example, the system described by Belshe et al. uses a replication competent vaccinia virus expressing T7 (Column 15 of Belshe), but it does not specify how a viable PIV virus would be recoverable in the presence of a vast excess of fully infectious, replication-competent vaccinia virus. It is unlikely that a low concentration of a recombinant PIV could be biologically separated from the replication-competent vaccinia. This is especially true since vaccinia virus is highly permissive for most cell types and is extremely difficult to fully neutralize with antibody. In contrast, in the methods described in the instant disclosure recognize and employ a replication deficient vaccinia virus (MVA-T7). This adaptation permitted the successful recovery of a recombinant PIV in the presence of the MVA-T7. Thus, Belshe et al. did not describe a system that would have been considered capable of successfully recovering recombinant PIV from cDNA, particularly attenuated (or attenuated, chimeric) viruses having further restrictions on replication.

24. The complexities and uncertainties that we had to overcome to achieve successful recovery of PIV from cDNA is further evinced by the extensive work involved in the recovery of other infectious recombinant negative strand RNA viruses. The general strategy that has proven successful is to reconstruct the viral nucleocapsid intracellularly from plasmid-expressed components. This is based on the idea that the nucleocapsid, i.e. the genome complexed with the nucleocapsid and polymerase proteins, constitutes the minimum unit of infectivity, a concept that dates back at least as far as 1967 (Brown et al. 1967 *J. Virol.* 1:368). In 1990, Ballart et al (Ballart et al 1990 *EMBO J.* 9:379) constructed a complete cDNA expressing the genome of measles virus under the control of a T7 promoter and reported the recovery of recombinant measles virus by complementation of this synthetic genome with intracellularly-expressed measles virus proteins. Although this report proved to be erroneous and was retracted (Eschle et al, 1991 *EMBO J.* 10:3558), this work outlined important general concepts for recovery. However, it is noteworthy that, despite considerable research effort on this high profile project, successful recovery of recombinant measles virus was not reported until December, 1995 (Radecke et al, 1995 *EMBO J.* 14:5773), a 5- to 6-year gap that reflects the formidable technical and conceptual challenges that must be met to achieve a successful recovery system. During that period, there was genuine concern that successful recovery of any negative strand virus might not be feasible. Thus, the successful recovery of recombinant rabies rhabdovirus in 1994 was a major milestone (Schnell et al 1994 *EMBO J.* 13:4195). However, it was not clear whether this would be successful with

paramyxoviruses, which have substantially greater genome size and complexity, more complex sets of protein products, and poorer growth and stability. In work with a second virus, the highly efficient rhabdovirus vesicular stomatitis virus (VSV), it was shown in 1990 that plasmid-expressed proteins could support a biologically derived nucleocapsid (Pattnaik et al, 1990 *J. Virol.* 64:2948), but two more years were required to develop the capability to express a defective interfering particle from cDNA (Pattnaik et al, 1992 *Cell* 69:1011). Three more years were required to express complete infectious recombinant virus (Lawson et al 1995 *Proc. Natl. Acad. Sci. USA* 92:4477; Whelan et al, 1995 *Proc. Natl. Acad. Sci. USA* 92:8388), which also was viewed as a major achievement (Roberts and Rose 1998 *Virology* 247:1). The work with the rhabdoviruses rabies and VSV involved unexpected requirements, such as the need to express the genome in positive sense form, the need to avoid structures causing early termination by the T7 RNA polymerase, and the need to reduce the background of vaccinia virus. In many instances, recovery depended on methods that could not be applied generally to other viruses, such as removal of the vaccinia virus background by filtration (Schnell et al 1994 *EMBO J* 13:4195, Lawson et al, ibid), which could not be applied to paramyxoviruses because of their large size and hence necessitated the development of alternative strategies. Studies in other nonsegmented negative stranded viruses illustrate still other unexpected requirements, such as the need to express an additional protein, the M2-1 protein, to achieve successful recovery of human respiratory syncytial virus (Collins et al, 1999, *Virology* 259:251). This brief survey of the literature embraces only to a subset of studies I know to have been undertaken in large numbers of labs across the globe seeking to recover negative stranded RNA viruses from cDNA. Many of those labs that never came close to successful recovery, thus their efforts have gone unreported. In summary, myriad challenges have persisted in the art to development of a successful recovery system for PIV. These challenges underscore the deficiencies of Belshe et al., who provide only vague, generic concepts without documentary experimentation nor demonstration of a feasible recovery system for PIV. At the same time, the slow-developing state of the art, and the high level of unpredictability in the field, emphasize the unexpected nature of results provided within the instant disclosure.

**Table 3 – Characteristics of recovered PIV3 or recombinant chimeric PIV**

Characteristics of PIV3 or chimeric virus recovered from full-length cDNA	Described in Murphy	Described in Belshe et al.
Viable virus that is recovered from wild	Viruses recovered and wild	Recombinant wild type

type PIV3 cDNA and from cDNA with backbone of wild type PIV3 containing substitution of wild type PIV1 HN and F for PIV3 HN and F and is replication competent and immunogenic in vivo is characterized for properties.	type phenotype demonstrated	or chimeric virus not recovered and thus properties could not be determined
Viable attenuated virus is recovered from PIV3 cDNA containing attenuating mutations and from cDNA with backbone of attenuated PIV3 containing substitution of wild type PIV1 HN and F for PIV3 HN and F	Virus recovered and attenuation, immunogenicity, and efficacy demonstrated	Recombinant attenuated PIV3 or chimeric virus not recovered and thus properties could not be determined

25. Although Belshe et al. show that it is facile to prophetically describe a method for recovering recombinant PIV from cDNA, the actual successful recovery of recombinant PIV for use as a vaccine is far more complicated than indicated by the cited reference. The properties of the virus that make it a successful vaccine candidate must be described in detail in a representative assemblage of recombinant species, as provided by the instant disclosure. There are three possible consequences that can occur when one attempts to recover a wild type PIV3 or a chimeric recombinant virus from cDNA: (1) a recombinant virus is recovered that replicates to levels characteristic of wild type virus or indicative of attenuation; (2) a recombinant virus is recovered that contains one or more inadvertent and unknown sequence errors that render it defective in any of a number of ways; and (3) virus is not recovered, due either to one or more lethal sequence errors or some deficiency in the recovery strategy or conditions. When one introduces mutations into such a cDNA intended to attenuate the virus and thereby to render it useful as a vaccine candidate, at least four outcomes are possible: (1) one can increase the virulence of the virus; (2) one can incompletely attenuate the virus; (3) one can achieve a satisfactory level of attenuation such that a virus can be used as a vaccine; and (4) one can over-attenuate a virus or render it non-viable. The examples provided in the instant specification fulfill criterion 3 by providing a representative assemblage of recombinant viruses that are suitably attenuated for development as vaccine agents. In contrast, the disclosure of Belshe et al. fails to achieve any of the foregoing possibilities--by virtue of its failure to describe and enable a cDNA construct encoding a

recombinant PIV (see Table 1), for failing to recover infectious virus from cDNA (Table 2), and for the lack of testing and characterization of an infectious, recombinant virus (Table 3).

26. In fact, the Belshe et al. specification provides only a limited description concerning the use of a plasmid expressing a wild type PIV3 L protein to enhance replication of a JScp45 virus at a restrictive temperature of 39.5°C. This limited disclosure does not provide a reasonable scientific basis for the speculation by Belshe et al. that the L gene of cp45 possesses mutations that might be useful in a recombinant PIV vaccine virus derived from cDNA. The virus recovered by Belshe et al. after complementation with the L-encoding plasmid at the restrictive temperature was not changed or modified in any manner as contemplated by Applicants' disclosure. No cDNA constructs were designed and produced from which PIV3 wild type viruses could be recovered, and certainly no new constructs or recombinant viruses bearing a chimeric genome or antigenome, and/or specific, attenuating mutations were described or enabled. The absence of such disclosure in the Belshe et al. reference negates any "reasonable expectation for success" to achieve the presently claimed invention in either its independent or dependent aspects. This is especially clear when the particular results provided by the instant disclosure are appreciated, namely that it was shown to be possible to construct a panel of recombinant PIVs, including singly and multiply attenuated and chimeric viruses, from cDNA that are suitably attenuated and immunogenic for development as vaccine candidates.

27. Concerning the issue of enablement, the foregoing discussion clearly establishes that the application provides extensive description, guidance, and working examples that teach the skilled artisan how to make and use recombinant PIVs from cDNA in a manner that is reasonably correlated with the full breadth of the claims. Numerous recombinant PIVs are described and tested in accepted model systems. For example, the instant disclosure details five attenuating mutations from the cp45 mutant that are identified, incorporated, and directly characterized in a recombinant PIV of the invention. Three of these mutations, identified in three different genes (C, F, and L), were shown to specify temperature sensitive attenuating mutations, while two others were demonstrated to specify non-ts attenuating mutations. Through the use of our novel PIV recovery system, the ability of these mutations to independently confer the property of attenuation on a recombinant virus in the absence of other cp45 mutations was proven. These studies fully evince the general usefulness of these mutations for attenuating recombinant vaccine viruses, including chimeric recombinant vaccine viruses, of the invention. At the same time, these studies clearly establish that a skilled artisan, following the teachings of the instant disclosure, will be enabled to identify additional useful mutations for incorporation within

recombinant PIV vaccine viruses of the invention, without undue experimentation. In particular, the successful recovery of a representative assemblage of useful recombinant PIV vaccine candidates shown here provides strong motivation and clear, detailed guidance to render any such experimentation as needed to obtain additional species within the generic scope of the instant claims "reasonable" and attended by a high expectation of success. That certain species may be less optimal than others, or even inoperable, does not negate the broad utility and scope of the invention in this context. The poorly developed state of the art and high degree of unpredictability that existed prior to the current invention is no longer extant. On the contrary, these barriers have been lowered sufficiently that the skilled artisan, availed of the teachings of the instant specification, can practice the invention throughout its scope without such extensive and/or uncertain experimentation that would be considered "undue" or unreasonable.

28. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that I make these statements with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize validity of the application or any patent issuing thereon.

Date: 8/26/02 By: Brian R. Murphy, M.D.  
Brian R. Murphy, M.D.

B.R. Murphy

8/26/02



## CURRICULUM VITAE

Name: Brian R. Murphy, M.D.

Date and Place of Birth: July 17, 1942; New York, New York

Social Security Number: 128-34-5897

Citizenship: United States

Marital Status: Married; two children

Address: Home: 5410 Tuscarawas Road  
Bethesda, MD 20816  
(301) 229-8564

Office: RVS/LID/NIAID/NIH  
Building 50, Room 6517  
50 South Drive MSC 8007  
Bethesda, MD 20892-8007  
Tele.: (301) 594-1616  
FAX: (301) 496-8312  
FAX: (301) 480-5033  
E-mail: bm25f@nih.gov

### Education:

June, 1960 Graduated from High School

June, 1964 B.A., Wesleyan University, Connecticut

June, 1969 M.D., University of Rochester, School of Medicine

### Brief Chronology of Employment:

1966 - 1967 Student Fellow, School of Medicine, University of Rochester,  
Department of Microbiology

1969 - 1970 Internship, Stanford University Hospital, Palo Alto, California

1970 - 1983 Research Associate, Laboratory of Infectious Diseases, NIAID,  
NIH, Bethesda, Maryland

1983 - 2001 Head, Respiratory Viruses Section, Laboratory of Infectious Diseases, National

2001- present      Co-Chief, Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland

**Military Service:**

1970 - 1998      United States Public Health Service

**Societies:**

Alpha Omega Alpha  
American Society for Microbiology  
Infectious Diseases Society  
American Society for Virology

**U.S. Patents:**

Title: TEMPERATURE-SENSITIVE RECOMBINANT MUTANT VIRUSES AND A PROCESS FOR PRODUCING SAME  
Inventors: Robert M. Chanock, Brian R. Murphy  
Patent No. 3,992,522  
Date: November 16, 1976

Title: USE IN AN ANIMAL HOST AND PRECURSORS FOR VACCINES UTILIZING AVIAN-HUMAN REASSORTANTS TO COMBAT INFLUENZA A  
Inventors: Brian R. Murphy, Robert M. Chanock, Robert G. Webster, Virginia S. Hinshaw  
Patent No. 4,552,757  
Date: November 12, 1985

Title: HUMAN USE OF AVIAN-HUMAN REASSORTANTS AS VACCINES FOR INFLUENZA A VIRUS  
Inventors: Brian R. Murphy, Robert M. Chanock, Robert G. Webster, Virginia S. Hinshaw  
Patent No. 4,552,758  
Date: November 12, 1985

Title: HUMAN NEUTRALIZING MONOCLONAL ANTIBODIES TO RESPIRATORY SYNCYTIAL VIRUS  
Inventors: Dennis R. Burton, Carlos F. Barbas, III, Robert M. Chanock, Brian R. Murphy, James E. Crowe, Jr.  
Patent No. 5,762,905  
Issued: June 9, 1998

Title: ATTENUATED RESPIRATORY SYNCYTIAL VIRUS VACCINE COMPOSITIONS  
Inventors: Brian Murphy, Robert Chanock, James Crowe, Jr., Mark Connors  
Patent No.: U.S. 5,922,326  
Date: July 13, 1999

Title: PRODUCTION OF ATTENUATED RESPIRATORY SYNCYTIAL VIRUS VACCINES FROM CLONED NUCLEOTIDE SEQUENCES

Inventors: Brian R. Murphy, Peter L. Collins, Stephen S. Whitehead, Alexander A. Bukreyev, Katalin Juhasz, Michael N. Teng

Patent No.: 5,993,824

Issued: Nov. 30, 1999

Title: IMMUNOGENIC COMPOSITIONS COMPRISING COLD-ADAPTED ATTENUATED RESPIRATORY SYNCYTIAL VIRUS MUTANTS

Inventors: Brian Murphy, Robert Chanock, James Crowe, Jr., Mark Connors, K-H L Hsu, A.R. Davis, M.D. Lubeck, B.H. Selling

Patent No.: 6,284,254 B1

Issued: Sept. 4, 2001

**Member of Editorial Board and/or Reviewer for the Following Journals:**

Reviewer of manuscripts for the following journals:

Antiviral Research

Archives of Virology

Clinical Microbiological Review

Journal of Clinical Investigation

Journal of Clinical Microbiology (editorial board),

Journal of Experimental Medicine

Journal of General Virology

Journal of Infectious Diseases

Journal of Immunology

Journal of Virology (editorial board)

New England Journal of Medicine

Proceedings of the National Academy of Sciences USA

Science

Vaccine

Virology

**Honors and Other Special Scientific Recognition:**

Edwin G. Strasenburgh Award, Rochester Academy of Medicine, 1967, 1969

Doctor of Medicine, with distinction in research

Consultant, World Health Organization at Meeting of Directors of WHO Respiratory Virus and Enterovirus Reference Center, April 16-19, 1973

Participant in a Symposium on Vaccination Against Influenza, London, April 1975

Invited speaker at ASM Conference on Myxovirus Genetics, Tampa, Florida, March 6-8, 1977

Invited participant at the Directors of the WHO Collaborating Centers for Virus Reference and Research Meeting, June 6-10, 1977

Invited participant in the International Association for Biological Standardization Meeting on Influenza Vaccines in Geneva, Switzerland, June 1977

Recipient of the PHS Commendation Medal, 1977

Invited speaker at the Symposium on the Advances in Vaccination against Virus Diseases in Bern, Switzerland, June 1978

Invited speaker, Royal Society Symposium on Influenza Virus Genetics, London, England, February 21 and 22, 1979

Invited speaker, New York Academy of Sciences Conference on Genetic Variation of Viruses, November, 1979

Chairman, ASM Seminar on Viral Vaccines of the Future, Miami, Florida, May 1980

Consultant on Influenza Vaccines, World Health Organization, November 1980

Invited speaker, ICN-UCLA Conference on the Genetic Variation of Influenza Viruses, Salt Lake City, Utah, March 1981

Invited speaker, Vaccination Against Influenza; T or B Cell Immunity, Oxford England, March 1982

Invited speaker, "Molecular Virology and Epidemiology of Influenza" (in celebration of 50 years of research on the Influenza Viruses) Hampstead, London, September 1983

Invited speaker, Cold Spring Harbor Conference on "Modern Approaches to Vaccines," Cold Spring Harbor, New York, September 1983

Keynote speaker, Eastern Chapter of American Society of Microbiology, Philadelphia, Pennsylvania, February 1985

Recipient of PHS Meritorious Service Medal, May 1985

Editorial board, *Journal of Clinical Microbiology*, January 1986-present

Convenor, American Society for Microbiology, "Viral Vaccines: Development and applications," Washington, DC, March 26, 1986

Consultant to U.S. Army Medical Research Institute of Infectious Diseases, "VEE Vaccines for Man," Fort Detrick, Maryland, December 1986

Co-inventor, United States Patent (number pending) Temperature sensitive reassortant viruses and vaccine against equine influenza, February 1987

Invited lecturer at Johns Hopkins School of Medicine, University of Maryland at College Park, and University of Maryland School of Medicine, Baltimore, MD and Mount Sinai Medical Center, and Uniformed Services University of the Health Sciences, 1987-1990.

Consultant, World Health Organization, 1987

State-of-the-Art lecture at the American Society of Virology meeting, Chapel Hill, North Carolina, June 1987

Chairman, Vaccines II session, American Society of Virology meeting, Chapel Hill, North Carolina, June 1987

Invited speaker at the Orthomyxovirus Symposium held at the VII International Congress of Virology, Edmonton, Canada, August 1987

Invited speaker at the "Oral Immunization Symposium" held in Birmingham, Alabama March 21, 1988

Invited speaker at Stanford University's lecture series on "Molecular and Genetic Medicine - Molecular Responses to Virus Infection" on May 2, 1988

Recipient of the United States Public Health Service Outstanding Service Medal, June 6, 1988.

Invited to present summary of the Vaccines 88 meeting held at Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, September, 1988

Appointed to the World Health Organization Steering Committee on Respiratory Viruses, 1988-1994.

Editorial Board, *Journal of Virology*, January 1, 1989 to 1994

Invited speaker at Conference on Emerging Viruses: Evolution of Viruses and Viral Diseases, sponsored by NIAID, Fogarty International Center, and the Rockefeller University, Washington, DC, May 1-3, 1989

Chairman of session on Vectors and Vaccines at a Symposium on Respiratory Virus Vaccine Development, sponsored by the World Health Organization, Washington, DC, May 1, 1989

Appointed Chairman of the World Health Organization Steering Committee on Respiratory Viruses and Measles, August 1989-1992.

Guest lecturer at the Department of Pediatrics at Vanderbilt University, July 18, 1989

Guest lecturer at the State University of New York at Buffalo, New York, September 16, 1989

Guest lecturer at the University of Maryland, School of Medicine, Department of Pediatrics, November 1989

Guest lecturer at Johns Hopkins University Department of Immunology, February 5, 1990

Chairman of session on Virology, Vaccines 89 symposium held at Cold Spring Harbor

Laboratory, Cold Spring Harbor, NY, September 1989

Invited to present lecture for the plenary session of the VIth International Conference on Comparative and Applied Virology, Banff, Alberta, Canada, October 15-21, 1989

Invited to review the Discovery Program of the Biotechnology and Microbiology Division of Wyeth-Ayerst Research, November 9-10, 1989

Visiting Research Professor at Children's Hospital National Medical Center, April 2, 1990

Co-organizer of WHO meeting on "New approach to measles virus vaccine" May 25-26, 1990

Invited to present lecture "RSV Vaccines" University of Massachusetts Medical School, Worcester, MA, October 3, 1990

Co-organizer of meeting on RSV vaccines, "Animal Models of RSV." Foundation Merieux, Annecy, France, October 23-25, 1990

Guest lecturer at the University of Maryland, October 1990-1993; Foundation for Advancement of Sciences at NIH course on Virology, Uniformed Services University of the Health Services, January, 1991; NIAID Immunology Course, February, 1991; NIAID Program "Introduction to Biomedical Research," February 1991.

Invited to give seminar "Current status of live attenuated influenza vaccines" January 10-11, 1991. Department of Immunology and Medical Microbiology, University of Florida.

Invited to present lecture "Influenza Viruses" to Department of Immunology and Infectious Diseases, Johns Hopkins University, February 13, 1991.

Invited to present a talk and chair a discussion section at the Poxvirus Vectors for HIV Vaccines held at NIH on August 22, 1991 on "Experiments to be conducted to evaluate safety/immunogenicity."

Invited speaker, "General Overview of Viral Vaccine Development," presented at conference entitled "Genetically Engineered Vaccines: Prospects for Oral Disease Prevention," National Institute of Dental Research, November 6, 1991.

Invited speaker, "The Use of Chimpanzees in Respiratory Virus Research," presented at a conference on "Chimpanzee Conservation and Public Health: Environments for the Future, sponsored by Diagnon Corporation, Rockville, MD, November 11, 1991.

Invited speaker, "The Development of Live Attenuated Influenza A Virus Vaccines," for NIAID Grand Rounds, National Institutes of Health, November 20, 1991.

Organizer of the WHO Meeting of RSV and PIV3 Vaccines, Geneva, Switzerland, April 21-22, 1992.

Invited participant, Buffalo Conference on Microbial Pathogenesis, Buffalo, NY, April 29, 1992.

Invited lecturer, Case Western Reserve University Institute of Pathology, Immunology Seminar Series, Cleveland, Ohio, May 5, 1992.

Recipient of Federal Laboratory Consortium Award on Technology Transfer for 1992.

Chairman of session on Vaccines, The Annual Meeting of the American Society of Virology, Ithaca, NY, July 1992.

Scientific Advisory Board, AVIRON, Palo Alto, CA, 1992 - 1993.

Member of NIAID Animal Care and Use Committee, 1989 - 1993.

Member of NIAID Technology Evaluation Advisory Committee, 1991 - Present.

Member of NIH ACUC Containment Housing for Research Animals Subcommittee, 1992.

Member of NIH Interagency Animal Model Committee (Infectious Diseases Subcommittee).

Chairman, Session on Bacteriology and Parasitology at the Cold Spring Harbor Meeting on "Modern Approaches to New Vaccines," September 16-20, 1992.

Chairman, Wyeth Ayerst-LID/NIAID Cooperative Research and Development Agreement Committee on the Development of Live Attenuated Respiratory Syncytial Virus Vaccines, 1992-Present.

Speaker at the NIH Clinical Center Grand Rounds on "Vaccines for Influenza," September 23, 1992.

Invited speaker, Johns Hopkins Pediatric Vaccine Seminar Series.

Member, NIH Institutional Biosafety Committee, 1993 - 1997.

Invited speaker, Keystone Symposia - Molecular Immunology of Virus Infections, Taos, NM, March 1993.

Invited speaker at WHO-NIAID meeting, Bethesda, MD, "Protective and Disease Enhancing Immune Response to RSV," May 1993.

Invited speaker at the American Society of Virology Satellite Symposium on Medical Virology on "Immunobiology of RSV Infection and Immunization," July, 1993, Davis, CA.

Workshop Co-chairman on Respiratory Viruses, IXth International Congress of Virology, Glasgow, August 1993.

Consultant for Genetic Therapies, Inc., September, 1993.

Invited speaker, St. Jude's Children's Hospital Virology Seminar Series, "Immunobiology of RSV," October 1993.

Organizer of WHO Meeting on Development of Vaccines Against Diseases Caused by RSV and PIV3, Nyon, Switzerland, March 27, 1994.

Invited speaker, Experimental Biology 94th Symposium, *Mucosal Vaccines: Recent Developments in Design and Human Analysis*, talk entitled "Mucosal Immunity to Respiratory Viral Infections," Anaheim, California, 1994.

Member, Search Committee for Chief, Division of Viral Products, FDA, CBER, 1994.

Invited speaker, Australian Society for Microbiology, presented the Bazely Oration entitled "Immunization against Respiratory Viruses," Melbourne, Australia, September 26, 1994.

Invited speaker, Australian Society for Microbiology Symposium on "Respiratory Viruses: Epidemiology and Control" talk entitled "Vaccines for Respiratory Syncytial Virus and Parainfluenza Virus Type 3," Melbourne, Australia, September 29, 1994.

Chairman of Session on "Virology," at the Meeting "Molecular Approaches to the Control of Infectious Diseases," Cold Spring Harbor, NY, October 5-9, 1994.

Scientific Advisory Board, Albert B. Sabin Vaccine Foundation, 1994.

Invited speaker, The Eastern Pennsylvania Branch of the American Society for Microbiology Symposium on "Vaccines: Preventive Strategies for the 21st Century." Talk entitled: "The Development and Evaluation of Live Attenuated Respiratory Syncytial Virus Vaccines," Philadelphia, PA, December 8-9, 1994.

Invited speaker, Keystone Symposia on Molecular Aspects of Viral Immunity. Talk entitled "Progress Toward the Development of a Live Attenuated Respiratory Syncytial Virus (RSV) Vaccine," Keystone, CO, January 16-23, 1995.

Co-chairperson of a Workshop on "Retroviral Screening, Sensitivity and Specificity" at FDA/CBER Meeting on "International Scientific Conference on Viral Safety and Evaluation of Viral Clearance from Biopharmaceutical Products" held at NIH, Bethesda, MD, June 14-16, 1995.

Presented "State-of-the-Art" Minilecture on "New Developments in Respiratory Virus Vaccines" at the 35th Interscience Conference on Antimicrobial Agents and Chemotherapy, San Francisco, CA, September 19, 1995.

Co-Organizer of "Workshop III -- Vaccines Against Respiratory Diseases" and Presenter of a lecture on "Two live attenuated parainfluenza virus type 3 (PIV3) candidate vaccines are safe, genetically stable, and immunogenic in seronegative infants and young children" at "Vaccines, One Hundred Years After Louis Pasteur," Institute Pasteur, Paris, France, September 24-28, 1995.

Invited speaker, NIH Grand Rounds on Influenza Virus Vaccines, November 1, 1995.

Invited speaker, Department of Microbiology and Immunology of the University of North Carolina at Chapel Hill Seminar Series. Talk entitled: "New Genetically Engineered Vaccines for Influenza A Viruses" November 16, 1995.

Invited speaker, On Pandemic Influenza -- Confronting a Re-Emergent Threat. Talk entitled: "Live Virus Vaccines" December 11-13, 1995.

NIAID Principle Investigation on NIH-Wyeth Lederle Pediatric Vaccines CRADA on Parainfluenza Virus type 3 vaccine development.

Member of NIAID Promotions and Tenure Committee, 1996 - 1999.

Invited lecturer on Influenza Virus Vaccine Development for a course "Biologic Basis of Vaccine Development" at the Johns Hopkins School of Hygiene and Public Health, Baltimore MD, May, 3, 1996.

Invited lecturer on Progress with RSV and Parainfluenza Virus Vaccine Development at the ATCC Seminar Co-organizer of WHO-NIAID Conference on RSV and PIV3 Vaccines held at NIH, Sept 30-Oct 1, 1996.

Invited to present a talk entitled "Vaccine Viruses of the Future" at the 1996 Medical Scientific Day Confere Appointed to the Malaria Vaccines Development Unit Scientific Advisory Board, 1997.

Co-Organized the NIH-WLVP RSV-PIV3 CRADA Meeting in Pearl River, NY on February 11 -12, 1997.

Co-Organized the NIH-WLVP RSV-PIV3 CRADA Meeting in Pearl River, NY on February 22 -24, 1998.

Invited participant in workshop on the "Appearance of H5N1 in humans" sponsored by the Institute of Immu Invited speaker at Conference on Mucosal Immunology and Medicine in St. Lucia on

March 17-18, 1998. Talk entitled: "Paramyxovirus vaccines for the early 21st century."

Invited speaker at a workshop on "Structure and Replication of Negative Strand RNA Viruses" held at North Invited speaker at the Research Triangle Virology Group Meeting in Raleigh, NC on September 9, 1998. Tal

Participant at an NIAID meeting on Influenza Virus Pandemic Planning on September 29-30, 1998, in Rock Invited speaker, International Symposium on Influenza and other Respiratory Viruses, talk

entitled "Molecular approaches to the generation of RSV and PIV vaccines," Dec. 4-6, 1998, Maui, Hawaii.

Invited speaker. Vaccine Research Center Discussion Group. Lecture entitled "Molecular approaches to the generation of RSV and PIV vaccines," Jan. 26, 1999, NIH, Bethesda, Maryland.

Invited speaker; Rudi Kasel Memorial Lecture. Talk entitled "Molecular approaches to the development of p Invited speaker; Keystone Symposia on Molecular Approaches to Human Viral Vaccines. Talk

entitled "Parainfluenza: Traditional versus molecular approaches to live virus vaccine development," April 12-17, 1999.

Invited to participate as a State-of-the-Art lecturer, 18<sup>th</sup> Annual Meeting of the American Society for Virology, Amherst, Massachusetts. Talk entitled "Molecular approaches to developing vaccines to parainfluenza viruses," July 10-14, 1999.

Invited to present a lecture on "Live attenuated virus vaccines: Preclinical Aspects" at the "II International Symposium on Influenza and Other Respiratory Virus Vaccines" held in Grand Cayman, Cayman Islands, December 10-12, 1999. Member of the Scientific Advisory Committee for the meeting.

Invited to participate in the NIH "Clinical Center Roundtable" broadcast on "Frontiers in Immunization - New and Improved Vaccines," December 17, 1999.

Invited speaker, "The Third Annual Conference on Vaccine Research." Talk entitled "Respiratory Syncytial Virus Vaccines." May 2, 2000, Washington DC.

Invited speaker at a symposium entitled "Pediatric Immunization. The Next Steps." Talk entitled "Recent Development of Live Attenuated Strains of Parainfluenza and Respiratory Syncytial Virus Vaccines." May 18, 2000, Chapel Hill, North Carolina.

Invited convener at the American Society of Virology Workshop #7, Paramyxoviruses and Bornaviruses: Replication. July 8, 2000, Fort Collins, Colorado.

Member of Scientific Advisory Committee for the "III International Symposium on Respiratory Viral Infections," December 1-3, 2000 in St. Lucia, Windward Island. Presented talk entitled "What are the diseases requiring vaccines and what is available."

Invited speaker on "Live viral (parainfluenza) vectored measles vaccines" at meeting entitled "Consultation of new measles virus vaccine candidates" on Mar. 22, 2001, Johns Hopkins University, Baltimore, MD.

Invited participant or the ACIP Influenza Working Group Meeting in Decatur, GA, May 9-10, 2001.

Invited speaker at ASM Colloquium on Live Engineered Vaccines at American Society for Microbiology 101th General Meeting, Orlando, Florida, May 22, 2001. Talk entitled "Molecular approaches to making live attenuated flavivirus vaccines".

Invited participant, NIAID Reverse Genetics Workshop, Georgetown, Washington, D.C. July 9-10, 2001.

Invited Consultant to the FDA for the Vaccines and Related Biological Products Advisory Committee Meeting for evaluation of the "Influenza Virus Vaccine, Trivalent, Types A and B, Live, Cold-Adapted in Rockville, MD on July 26-27, 2001. Presented talk concerning "Overview of Development of Cold-adapted, Live Attenuated Influenza Vaccines; Basis of Attenuation; and Potential for Reassortment with Wild-type Viruses in Nature.

Invited speaker, "Influenza Viruses – Medicine for the Public", NIH, Oct. 30, 2001.

Invited panel participant, NIAID Blue Ribbon Panel on Terrorism and its Implications for Biomedical Research, NIH, Feb. 4-5, 2002.

B.R. Murphy



8/26/02

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## BIBLIOGRAPHY

1. Murphy BR, Glasgow LA. Factors modifying host resistance to viral infection. III. Effect of whole body X-irradiation on experimental encephalomyocarditis virus infection in mice. *J Exp Med* 1968;127:1035-1052.
2. Murphy BR, Glasgow LA. Factors modifying host resistance to viral infection. I. Effect of immunosuppressive drugs on experimental infection of mice with encephalomyocarditis virus. In Hobby GL, ed. *Antimicrobial Agents and Chemotherapy*. Ann Arbor, MI: American Society of Microbiology 1969;661.
3. Murphy BR, Glasgow LA. The antiviral activity of 3, 4-dehydro-1-isoquinolineacetamide hydrochloride on Columbia SK virus infection in mice and tissue culture. *Ann NY Acad Sci* 1970;173:225-273.
4. Murphy BR, Kasel JA, Chanock RM. Association of serum anti-neuraminidase antibody with resistance to influenza in man. *N Engl J Med* 1972;286:1329-1332.
5. Murphy BR, Chalhub EG, Nusinoff SR, Chanock RM. Temperature-sensitive mutants of influenza virus. II. Attenuation of *ts* recombinants for man. *J Infect Dis* 1972;126:170-178.
6. Murphy BR, Chalhub EG, Nusinoff SR, Chanock RM. Temperature-sensitive mutants of influenza virus. III. Further characterization of the *ts*-1[E] influenza A recombinant (H3N2) virus in man. *J Infect Dis* 1973;128:479-487.
7. Murphy BR, Baron S, Chalhub EG, Uhlendorf CP, Chanock RM. Temperature-sensitive mutants of influenza virus. IV. Induction of interferon in the nasopharynx by wild-type and a temperature-sensitive recombinant virus. *J Infect Dis* 1973;128:488-493.
8. Parrott RH, Kim HW, Arrobo JO, Hodes DS, Murphy BR, Brandt CD, Camargo E, Chanock RM. Epidemiology of respiratory syncytial virus infection in Washington, D.C. II. Infection and disease with respect to age, immunologic status, race, and sex. *Am J Epidemiol* 1973;98:289-300.
9. Murphy BR, Hodes DS, Nusinoff SR, Spring-Stewart S, Tierney EL, Chanock RM. Temperature-sensitive mutants of influenza virus. V. Evaluation in man of an additional *ts* recombinant virus with a 39°C shutoff temperature. *J Infect Dis* 1974;130:144-149.
10. Richman DD, Murphy BR, Tierney EL, Chanock RM. Specificity of the local secretory antibody to influenza A virus infection. *J Immunol* 1974;113:1654-1656.
11. Chanock RM, Richman DD, Murphy BR, Spring SB, Schnitzer TS, Richardson LS. Current approaches to viral immunoprophylaxis. In Notkins AL, ed. *Viral Immunology and Immunopathology*. New York: Academic Press 1975;291-316.

12. Murphy BR, Richman DD, Chalhub EG, Uhlendorf CP, Baron S, Chanock RM. Failure of attenuated temperature-sensitive influenza A (H3N2) virus to induce heterologous interference in humans to parainfluenza type 1 virus. *Infect Immun* 1975;12:62-68.
13. Murphy BR, Spring SB, Richman DD, Tierney EL, Kasel J, Chanock RM. Temperature-sensitive mutants of influenza virus. VII. Transfer of the *ts*-1[E] lesions to a wild-type influenza A virus with the HON1 surface antigens. *Virology* 1975;66:533-541.
14. Richman DD, Murphy BR, Cline WC, Alling DW. Determination of influenza virus neuraminidase inhibition titres. *Bull WHO* 1975;52:233-234.
15. Richman DD, Murphy BR, Spring SB, Coleman MT, Chanock RM. Temperature-sensitive mutants of influenza virus. IX. Genetic and biological characterization of *ts*-1[E] lesions when transferred to a 1972 (H3N2) influenza A virus. *Virology* 1975;66:551-562.
16. Spring SB, Nusinoff SR, Mills JV, Richman DD, Tierney EL, Murphy BR, Chanock RM. Temperature-sensitive mutants of influenza virus. VI. Transfer of *ts* lesions from the Asian subtype of influenza A virus (H2N2) to the Hong Kong subtype (H3N2). *Virology* 1975;66:522-532.
17. Spring S, Nusinoff S, Tierney EL, Richman DD, Murphy BR, Chanock RM. Temperature-sensitive mutants of influenza virus. VIII. Genetic and biological characterization of *ts* mutants of influenza virus A (H3N2) and their assignment to complementation groups. *Virology* 1975;66:542-550.
18. Douglas RG Jr, Bentley DW, Betts RR, Zaky DA, Roth FK, Murphy BR. Evaluation of a temperature sensitive influenza virus in elderly and chronically ill subjects. *Am Rev Respir Dis* 1976;113:293-300.
19. Hall WJ, Douglas RG Jr, Zaky DA, Hyde RW, Richman DD, Murphy BR. Attenuated influenza virus in normal adults: The role of pulmonary function studies in vaccine trials. *J Infect Dis* 1976;133:145-152.
20. Kim HW, Arrobio JO, Brandt CD, Parrott RH, Murphy BR, Richman DD, Chanock RM. Temperature-sensitive mutants of influenza A virus: response of children to the influenza A/Hong Kong/68-*ts*-1[E](H3N2) and influenza A/Udorn/72-*ts*-1[E] (H3N2) candidate vaccine viruses and significance of immunity to neuraminidase antigen. *Pediatr Res* 1976;10:238-242.
21. Murphy BR, Richman DD, Spring SB, Chanock RM. Recent progress in the development and assessment of live attenuated vaccines. Use of temperature-sensitive mutants of influenza A virus as live virus vaccine strains -- Evaluation in laboratory animals, adults, and children. *Postgrad Med J* 1976;52:381-388.
22. Murphy BR, Spring SB, Chanock RM. Live vaccine: production and use. In Selby P, ed. *Influenza: Virus, Vaccines, and Strategy*. New York: Academic Press 1976;179-198.

23. Murphy BR, Tierney EL, Spring SB, Chanock RM. Temperature sensitive mutants of influenza A virus. XI. Transfer of *ts* lesions in the Hong Kong/68-*ts*-1[A] virus to the influenza A/Udorn/72 wild type. *J Infect Dis* 1976;134:577-584.
24. Richman DD, Murphy BR, Baron S, Uhlendorf CP. Three strains of influenza A virus (H3N2): Interferon sensitivity *in vitro* and interferon production in volunteers. *J Clin Microbiol* 1976;3:223-226.
25. Richman DD, Murphy BR, Chanock RM, Gwaltney JM, Douglas RG Jr, Betts RF, Blacklow NR, Rose FB, Parrino TA, Levine MM, Caplan ES. Temperature-sensitive mutants of influenza A virus. XII. Safety, antigenicity, transmissibility, and efficacy of influenza A/Udorn/72-*ts*-1[E] recombinant viruses in human adults. *J Infect Dis* 1976;134:585-594.
26. Chanock RM, Murphy BR, Spring SB, Richman DD. Live virus vaccines for use in humans: Strategies and problems. Rationale for the development of live virus vaccines by use of temperature-sensitive mutants. In Younger JS, ed. *Microbiology*. American Society for Microbiology 1977;516-520.
27. Chanock RM, Murphy BR, Spring SB, Markoff LJ, Richardson LS, Belshe RB. The use of live mutants for the prevention of respiratory tract disease. *Acta Pathol et Microbiol Scand* 1977.
28. Dolin R, Richman DD, Murphy BR, Fauci AS. Cell-mediated immune responses in humans after induced infection with influenza A virus. *J Infect Dis* 1977;135:714-719.
29. Easterday BC, Murphy BR, McGregor S. Infection and vaccination of pigs with A/New Jersey/8/76 (Hsw N1) virus. *J Infect Dis* 1977;136:S699-702.
30. Kendal AP, Cox NJ, Murphy BR, Spring SB, Maassab HF. Comparative studies of wild-type and 'cold-mutant' (temperature sensitive) influenza viruses: Genealogy of the matrix (m) and non-structural (ns) proteins in recombinant cold-adapted H3N2 viruses. *J Gen Virol* 1977;37:145-159.
31. Maassab HF, Cox NJ, Murphy BR, Kendal AP. Biological, genetic, and biochemical characterization of a cold-adapted recombinant A/Victoria/3/75 virus and its evaluation in volunteers. International symposium on influenza immunization (II), Geneva, 1977. *Develop Biol Stand* 1977;39:25-31.
32. Mostow SR, Flatauer S, Paler M, Murphy BR. Temperature-sensitive mutants of influenza virus. XIII. Evaluation of influenza A/Hong Kong/68 and A/Udorn/72 *ts* and wild type viruses in tracheal organ culture at permissive and restrictive temperatures. *J Infect Dis* 1977;136:1-6.
33. Murphy BR, Markoff LJ, Chanock RM, Douglas RG, Bett RF, Cate TR, Couch RB. An evaluation of influenza A/Victoria/3/75-*ts*-1[E] recombinant viruses for attenuation and immunogenicity in adult seronegative volunteers. International symposium on influenza immunization (II), Geneva, 1977. *Develop Biol Stand* 1977;39:47-52.

34. Richman DD, **Murphy BR**, Belshe RB, Rusten HM, Chanock RM, Blacklow NR, Parrino TA, Rose FB, Levine MM, Caplan E. Temperature-sensitive mutants of influenza A virus. XIV. Production and evaluation in volunteers of influenza A/Georgia/74-ts-1[E] recombinant viruses in human adults. *J Infect Dis* 1977;136:256-262.
35. Richman DD, **Murphy BR**, Chanock RM. Demonstration of a non-temperature-sensitive growth-restricting mutation in a *ts* mutant of influenza A virus: implications for live virus vaccine development. *Virology* 1977;83:356-364.
36. Spring SB, Maassab HF, Kendal AP, **Murphy BR**, Chanock RM. Cold-adapted variants of influenza A virus. I. Comparison of the genetic properties of *ts* mutants and five cold-adapted variants of influenza A virus. *Virology* 1977;77:337-343.
37. Spring SB, Maassab HF, Kendal AP, **Murphy BR**, Chanock RM. Cold-adapted variants of influenza A. II. Comparison of the genetic and biological properties of *ts* mutants and recombinants of the cold-adapted A/Ann Arbor/6/60 strain. *Arch Virol* 1977;55:233-246.
38. Dolin R, **Murphy BR**, Caplan EC. Lymphocyte blastogenic responses to influenza virus antigens after influenza infection and vaccination in humans. *Infect Immun* 1978;19:867-874.
39. Grizzard MB, London WT, Sly DL, **Murphy BR**, James WD, Parnell WP, Chanock RM. Experimental production of respiratory tract disease in cebus monkeys after intratracheal or intranasal infection with influenza A/Victoria/3/75 or influenza A/New Jersey/76 virus. *Infect Immun* 1978;201-205.
40. Massicot J, **Murphy BR**. Comparison of the hemagglutination-inhibiting and neutralizing antibody responses of volunteers given 400 chick cell-agglutinating units of influenza A/New Jersey/76 split-virus vaccine. *J Infect Dis* 1978;136:S472-S474.
41. **Murphy BR**, Hosier NT, Spring SB, Mostow SR, Chanock RM. Temperature-sensitive mutants of influenza A virus: Production and characterization of A/Victoria/3/75-*ts*-1[E] recombinants. *Infect Immun* 1978;20:655-670.
42. **Murphy BR**, Markoff LJ, Hosier NT, Rusten HM, Chanock RM, Kendal AP, Douglas RG, Betts RF, Cate TRJr, Couch RM, Levine MM, Waterman DH, Holley HPJr. Temperature-sensitive mutants of influenza A virus: Evaluation of A/Victoria/3/75-*ts*-[E] recombinant viruses in volunteers. *Infect Immun* 1978;20:671-677.
43. **Murphy BR**, Wood FT, Massicot JG, Chanock RM. Temperature- sensitive mutants of influenza virus: XVI. Transfer of the two *ts* lesions present in the Udorn/72-*ts*-1A2 donor virus to the Victoria/3/75 wild-type virus. *Virology* 1978;88:244-251.
44. **Murphy BR**, Wood FT, Massicot JG, Spring SB, Chanock RM. Temperature-sensitive mutants of influenza A virus. XV. The genetic and biological characterization of a recombinant influenza virus containing two *ts* lesions produced by mating two complementing, single lesion *ts* mutants. *Virology* 1978;88:231-243.

45. Scholtissek C, **Murphy BR**. Host range mutants of an influenza A virus. *Arch Virol* 1978;58:323-333.
46. Chanock RM, **Murphy BR**. Genetic approaches to control of influenza. *Persp Biol Med* 1979;22:S37-S48.
47. Douglas RGJr, Markoff LJ, **Murphy BR**, Chanock RM, Betts RF, Hayden FG, Levine MM, Van Blerk GA, Sotman SB, Nalin DR. Live Victoria/75-ts-1[E] influenza A virus vaccines in adult volunteers: role of hemagglutinin immunity in protection against illness and infection caused by influenza A virus. *Infect Immun* 1979;26:280-286.
48. Kim HW, Brandt CD, Arrobo JO, **Murphy BR**, Chanock RM, Parrott RH. Influenza A and B virus infection in infants and young children during the years 1957-1976. *Am J Epidemiol* 1979;109:464-479.
49. Markoff LJ, **Murphy BR**, Kendal AP, Chanock RM. Probable association of plaque size with neuraminidase subtype among H3N2 influenza A viruses. *Arch Virol* 1979;62:277-280.
50. Markoff LJ, Thierry F, **Murphy BR**, Chanock RM. Relationship of genotype of recombinants of influenza A/Hong Kong/68-ts-1[E] virus used as live virus vaccines to virulence in humans. *Infect Immun* 1979;26:280-286.
51. **Murphy BR**, Chanock RM. The present status of live influenza A virus vaccine. *Monogr Pediat* 1979;11:1-20.
52. **Murphy BR**, Chanock RM, Levine MM, Van Blerk GA, Berquist EG, Douglas RG, Betts RF, Couch RB, Cate TRJr. Temperature-sensitive mutants of influenza A virus: Evaluation of the Victoria/75-ts-1A2 temperature-sensitive recombinant virus in seronegative adult volunteers. *Infect Immun* 1979;23:249-252.
53. **Murphy BR**, Holley HPJr, Berquist EJ, Levine MM, Spring SB, Maassab HF, Kendal AP, Chanock RM. Cold-adapted variants of influenza A virus: evaluation in adult seronegative volunteers of A/Scotland/840/74 and A/Victoria/3/75 cold-adapted recombinants derived from the cold-adapted A/Ann Arbor/6/60 strain. *Infect Immun* 1979;23:253-259.
54. Reichman RC, Pons VG, **Murphy BR**, Caplan EA, Dolin R. Cell-mediated cytotoxicity following influenza infection and vaccination in humans. *J Med Virol* 1979;4:1-14.
55. Richman DD, **Murphy BR**. The association of the temperature-sensitive phenotype with viral attenuation in animals and humans: Implications for the development and use of live virus vaccines. *Rev Infect Dis* 1979;1:413-433.
56. Berg RA, Rennard SI, **Murphy BR**, Yolken RH, Dolin R, Straus SE. New enzyme immunoassays for measurement of influenza A/Victoria/3/75 virus in nasal washes. *Lancet* 1980;1:851-853.

57. Chanock RM, **Murphy BR**. Use of temperature-sensitive and cold-adapted mutant viruses in immunoprophylaxis of acute respiratory tract disease. *Rev Infect Dis* 1980;2:421-432.
58. Massicot JG, **Murphy BR**, Thierry F, Markoff L, Huang K-Y, Chanock RM. Temperature-sensitive mutants of influenza virus: Identification of the loci of the 2 *ts* lesions in the Udom-*ts*-1A2 donor virus and the correlation of the presence of these 2 *ts* lesions with a predictable level of attenuation. *Virology* 1980;101:242-249.
59. Massicot JG, **Murphy BR**, van Wyke K, Huang K-Y, Chanock RM. *TS* P1 and P3 genes are responsible for satisfactory level of attenuation of *ts*-1A2 recombinants bearing H1N1 or H3N2 surface antigens of influenza A virus. *Virology* 1980;106:187-190.
60. **Murphy BR**, Chanock RM, Douglas RG, Betts RF, Waterman DH, Holley HP, Hoover DL, Suwanagool S, Nalin DR, Levine MM. Temperature-sensitive mutants of influenza A virus: evaluation of the Alaska/77-*ts*-1A2 temperature-sensitive recombinant virus in seronegative adult volunteers. *Arch Virol* 1980;65:169-173.
61. **Murphy BR**, Hosier NT, Chanock RM. Temperature-sensitive mutants of influenza A virus: transfer of the two temperature-sensitive lesions in the Udom/72-*ts*-1A2 virus to the A/Hong Kong/123/77 (H1N1) wild-type virus. *Infect Immun* 1980;28:792-798.
62. **Murphy BR**, Markoff LJ, Chanock RM, Spring SB, Maassab HF, Kendal AP, Cox NJ, Levine MM, Douglas RGJr, Betts RF, Couch RB, Cate TRJr. Genetic approaches to attenuation of influenza A viruses for man. *Phil Trans R Soc Lond* 1980;B288:401-415.
63. **Murphy BR**, Rennels MB, Douglas RGJr, Betts RF, Couch RB, Cate TR Jr, Chanock RM, Kendal AP, Maassab HR, Suwanagool S, Sotman SB, Cisneros LA, Anthony WC, Nalin DR, Levine MM. Evaluation of influenza A/Hong Kong/123/77 (H1N1) *ts*-1A2 and cold-adapted recombinant viruses in seronegative adult volunteers. *Infect Immun* 1980;29:348-355.
64. **Murphy BR**, Sly DL, Hosier NT, London WT, Chanock RM. Evaluation of the three strains of influenza A virus in humans and in owl, cebus, and squirrel monkeys. *Infect Immun* 1980;28:688-691.
65. **Murphy BR**, Tierney EL, Barbour BA, Yolken RH, Alling DW, Holley HPJr, Mayner RE, Chanock RM. Use of the enzyme-linked immunosorbent assay to detect serum antibody responses of volunteers who received attenuated influenza A virus vaccines. *Infect Immun* 1980;29:342-347.
66. **Murphy BR**, Tolpin MD, Massicot J, Kim HW, Parrott RH, Chanock RM. Escape of a highly defective influenza A virus mutant from its temperature sensitive phenotype by extragenic suppression and other types of mutation. *Ann NY Acad Sci* 1980;354:172-182.
67. **Murphy BR**, Wood FT, Massicot JG, Chanock RM. Temperature-sensitive mutants of influenza A virus: Transfer of the two *ts*-1A2 *ts* lesions present in the Udom/72-*ts*-1A2 donor virus to the influenza A/Alaska/6/77 (H3N2) wild type virus. *Arch Virol* 1980;65:175-186.

68. Shimizu K, **Murphy BR**, Chanock RM. Temperature-sensitive mutants of influenza A/Udorn/72 (H3N2) virus: Intrasegmental complementation and temperature dependent host range (td-hr) mutation. In Compans RW, Bishop DHL, eds. *Negative Strand Viruses*. New York: Elsevier-North Holland 1980;369-378.
69. Yolken RH, Torsch VM, Berg R, **Murphy BR**, Lee YC. Fluorometric assay for measurement of viral neuraminidase-application to the rapid detection of influenza virus in nasal wash specimens. *J Infect Dis* 1980;142:516-523.
70. Daisy JA, Tolpin MD, Quinnan GV Jr, Rook AH, **Murphy BR**, Levine MM, Clements ML, Mittal K, Kjeu J, Ennis FA. Induction of cytotoxic T lymphocytic activity and augmentation of natural killer cell activity during influenza infection. In Compans RW, Bishop DHL, eds. *Negative Strand Viruses*. New York: Elsevier-North Holland 1981;443-448.
71. **Murphy BR**, Chanock RM. Genetic approaches to the prevention of influenza A virus infection. In Nayak D, Fox C, eds. *Genetic Variation Among Influenza Viruses*. ICN-UCLA Symposia on Molecular and Cellular Biology, Vol. 22. New York: Academic Press 1981;601-616.
72. **Murphy BR**, Chanock RM, Clements ML, Anthony WC, Sear AJ, Cisneros LA, Rennels MB, Miller EH, Black RE, Levine MM, Betts RF, Douglas RGJr, Maassab HF, Cox NJ, Kendal AP. Evaluation of A/Alaska/6/77 (H3N2) cold-adapted recombinant viruses derived from the A/Ann Arbor/6/60 cold-adapted donor virus in adult seronegative volunteers. *Infect Immun* 1981;32:693-697.
73. **Murphy BR**, Maassab HF, Wood FTJr, Chanock RM. A characterization of the temperature sensitive phenotype of the A/Ann Arbor/6/60 cold-adapted virus and recombinants derived from it. *Infect Immun* 1981;32:960-963.
74. **Murphy BR**, Phelan MA, Nelson DL, Yarchoan R, Tierney EL, Alling DW, Chanock RM. A hemagglutinin-specific enzyme-linked immunosorbent assay for antibodies to influenza A and B viruses. *J Clin Microbiol* 1981;13:554-560.
75. Tolpin MD, Massicot JG, Mullinix MG, Kim HW, Parrott RH, Chanock RM, **Murphy BR**. Genetic factors associated with loss of the temperature-sensitive phenotype of the influenza A/Alaska/77-ts-1A2 recombinant during growth *in vivo*. *Virology* 1981;112:505-517.
76. Tyrrell DAJ, Schild GC, Dowdle WR, Chanock RM, **Murphy BR**. Mise au point et utilisation des vaccins antigrippaux (Development and use of influenza vaccines). *Bull WHO* 1981;59:519-528.
77. Yarchoan R, **Murphy BR**, Strober W, Clements ML, Nelson DL. *In vitro* production of anti-influenza virus antibody after intranasal inoculation with cold-adapted influenza virus. *J Immunol* 1981;127:1958-1963.

78. Yarchoan R, **Murphy BR**, Strober W, Biddison WE, Blaese RM, Nelson DL. Anti-influenza antibody production *in vitro* by human peripheral blood mononuclear cells. In Reich K, Kirchner H, eds. *Mechanisms of Lymphocyte Activation*. Proceedings of the 14th Leukocyte Culture Conference. New York: Elsevier-North Holland 1981;677-679.
79. Yarchoan R, **Murphy BR**, Strober W, Schnieder HS, Nelson DL. Specific anti-influenza virus antibody production *in vitro* by human peripheral blood mononuclear cells. *J Immunol* 1981;127:2588-2594.
80. Brundage-Anguish LJ, Holmes DF, Hosier NT, **Murphy BR**, Massicot JG, Appleyard G, Coggins L. Live temperature-sensitive equine influenza virus vaccine: Generation of the virus and efficacy in hamsters. *Am J Vet Res* 1982;43:869-874.
81. Hobbins TE, Hughes TP, Rennels MB, Levine MM, **Murphy BR**. Bronchial reactivity in experimental infections with influenza virus. *J Infect Dis* 1982;146:468-71.
82. Massicot JG, van Wyke K, Chanock RM, **Murphy BR**. Evidence for intrasegmental complementation between two influenza A viruses having *ts* mutations on their P1 genes. *Virology* 1982;117:496-500.
83. **Murphy BR**, Hinshaw VS, Sly DL, London WT, Hosier NT, Wood FT, Webster RG, Chanock RM. Virulence of avian influenza A viruses for squirrel monkeys. *Infect Immun* 1982;37:1119-1126.
84. **Murphy BR**, Markoff LJ, Hosier NT, Massicot JG, Chanock RM. Production and level of genetic stability of an influenza A virus temperature-sensitive mutant containing two genes with *ts* mutations. *Infect Immun* 1982;37:235-242.
85. **Murphy BR**, Nelson D, Wright PF, Tierney EL, Phelan MA, Chanock RM. Secretory and systemic immunological response in children infected with live attenuated influenza A virus vaccines. *Infect Immun* 1982;36:1102-1108.
86. **Murphy BR**, Sly DL, Tierney EL, Hosier NT, Massicot JG, London WT, Chanock RM, Webster RG, Hinshaw VS. Reassortant virus derived from avian and human influenza A viruses is attenuated and immunogenic in monkeys. *Science* 1982;218:1330-1332.
87. Shimizu K, Mullinix MG, Chanock RM, **Murphy BR**. Temperature-sensitive mutants of influenza A/Udorn/72 (H3N2) virus. I. Isolation of temperature-sensitive mutants, some of which exhibit host dependent temperature sensitivity. *Virology* 1982;117:38-44.
88. Shimizu K, Mullinix MG, Chanock RM, **Murphy BR**. Temperature-sensitive mutants of influenza A/Udorn/72 (H3N2) virus. II. Genetic analysis and demonstration of intrasegmental complementation. *Virology* 1982;117:45-61.
89. Tolpin MD, Clements ML, Levine MM, Black RE, Saah AJ, Anthony WC, Cisneros L, Chanock RM, **Murphy BR**. Evaluation of a phenotypic revertant of the A/Alaska/7 *ts*-1A2 reassortant virus in hamsters and in seronegative adult volunteers: Further evidence that the temperature-sensitive phenotype is responsible for attenuation of *ts*-1A2 reassortant viruses. *Infect Immun* 1982;36:645-650.

90. Burlington DB, Clements ML, Meiklejohn G, Phelan M, **Murphy BR**. Hemagglutinin specific antibody responses in the IgG, IgA and IgM isotypes as measured by ELISA after primary or secondary infection of man with influenza A virus. *Infect Immun* 1983;41:540-545.
91. Clements ML, O'Donnell S, Levine MM, Chanock RM, **Murphy BR**. Dose response of A/Alaska/6/77 (H3N2) cold-adapted reassortant vaccine virus in adult volunteers; role of local antibody in resistance to infection with vaccine. *Infect Immun* 1983;40:1044-1051.
92. Hinshaw VS, Webster RG, Naeve CW, **Murphy BR**. Altered tissue tropism of human-avian reassortant influenza viruses. *Virology* 1983;128:260-263.
93. La Montagne JR, Wright PF, Clements ML, Maassab HF, **Murphy BR**. Prospects for live, attenuated influenza vaccines using reassortants derived from the A/Ann Arbor/6/60 (H2N2) cold-adapted (*ca*) donor virus. In Laver WG, ed. *Origins of Pandemic Influenza Viruses*. New York: Elsevier-North Holland 1983;243-257.
94. **Murphy BR**, Harper J, Sly DL, London WT, Miller NT, Webster RG. Evaluation of the A/Seal/Mass/1/80 virus in squirrel monkeys. *Infect Immun* 1983;42:424-426.
95. Shimizu K, Mullinix MG, Chanock RM, **Murphy BR**. Temperature-sensitive mutants of influenza A/Udorn/72 (H3N2) virus. III. Genetic analysis of temperature-dependent host range mutants. *Virology* 1983;124:35-44.
96. Smith GL, **Murphy BR**, Moss B. Construction and characterization of an infectious vaccinia virus recombinant that expresses the influenza hemagglutinin gene and induces resistance to influenza virus infection in hamsters. *Proc Natl Acad Sci USA* 1983;80:7155-7159.
97. Webster RG, Hinshaw VS, Naeve CW, Bean WJ, **Murphy BR**, Bigelow MA. Host range of influenza A viruses and potential new vaccines. Symposium on Influenza Virus. In Webster RA, ed. *Current Topics and Prospects in Influenza*. Valladolid, Spain: Spanish Society for Microbiology 1983;123-131.
98. Wright PF, **Murphy BR**, Kervina M, Lawrence EM, Phelan MA, Karzon DT. Secretory immunological response after intranasal inactivated influenza A virus vaccines: evidence for immunoglobulin A memory. *Infect Immun* 1983;40:1092-1095.
99. Clements ML, Betts RF, Maassab HF, **Murphy BR**. Dose response of influenza A/Washington/897/80 (H3N2) cold-adapted reassortant virus in adult volunteers. *J Infect Dis* 1984;149:814-815.
100. Chanock RM, **Murphy BR**, Lai C-J, Markoff LJ, Lin B-C. Prospects for stabilization of attenuation. In Stuart-Harris SC, Potter CW, eds. *Molecular Virology and Epidemiology of Influenza*. London: Academic Press 1984;237-256.

101. Clements ML, Betts RF, **Murphy BR**. Advantage of live attenuated cold-adapted influenza A virus over inactivated vaccine for A/Washington/80 (H3N2) wild-type virus infection. *Lancet* 1984;1:705-708.
102. **Murphy BR**, Buckler-White A, London WT, Harper J, Tierney EL, Miller NT, Reck LJ, Chanock RM, Hinshaw VS. Avian-human reassortant influenza A viruses derived by mating the A/Mallard/78 (H2N2) avian with a human H1N1 or H3N2 wild type virus. *J Infect Dis* 1984;150:841-850.
103. **Murphy BR**, Buckler-White AJ, Tian S-F, Clements ML, London WT, Chanock RM. Use of avian-human reassortant influenza A viruses as live vaccine viruses in man. In Compans RW, Bishop DHL, eds. *Segmented Negative Strand Viruses: Arenaviruses, Bunyaviruses, and Orthomyxoviruses*. New York: Academic Press 1984;395-405.
104. **Murphy BR**, Clements ML, Maassab HF, Buckler-White AJ, Tian S-F, London WT, Chanock RM. The basis of attenuation of virulence of influenza virus for man. In Stuart-Harris SC, Potter CW, eds. *The Molecular Virology and Epidemiology of Influenza*. London: Academic Press 1984;211-235.
105. **Murphy BR**, Clements ML, Maassab HF, Buckler-White AJ, Tian S-F, London WT, Chanock RM. Attenuation of wild-type influenza A viruses for man by genetic reassortment with attenuated donor viruses. In Chanock RM, Lerner RA, eds. *Modern Approaches to Vaccines: Molecular and Chemical Basis of Virus Virulence and Immunogenicity*. New York: Cold Spring Harbor Laboratory 1984;329-337.
106. **Murphy BR**, Clements ML, Madore HP, Steinberg J, O'Donnell S, Betts, Dolin R, Maassab HF. Dose response of cold-adapted, reassortant influenza A/California/10/78 (H1N1) in adult volunteers. *J Infect Dis* 1984;149:816.
107. Smith GL, Mackett M, **Murphy BR**, Moss B. Vaccinia virus recombinants expressing genes from pathogenic agents have potential as live vaccines. In Chanock RM, Lerner RA, eds. *Modern Approaches to Vaccines: Molecular and Chemical Basis of Virus Virulence and Immunogenicity*. New York: Cold Spring Harbor Laboratory 1984;313-317.
108. Tian S-F, Zhang L-X, **Murphy BR**. Characterization of the genotype and level of attenuation of an influenza A reassortant virus produced by mating the Xia-ts donor virus with A/Beijing/79 (H1N1) wild type virus. *Vaccine* 1984;2:189-192.
109. van Wyke KL, Yewdell JW, Michalek SM, McGhee JR, **Murphy BR**. Antigenic characterization of influenza A matrix protein with monoclonal antibodies. In Compans RW, Bishop DHL, eds. *Segmented Negative Strand Viruses: Arenaviruses, Bunyaviruses, and Orthomyxoviruses*. New York: Academic Press 1984;307-314.
110. van Wyke KL, Yewdell JW, Reck LJ, **Murphy BR**. Antigenic characterization of influenza A matrix protein with monoclonal antibodies. *J Virol* 1984;49:248-52.

111. Betts RF, Douglas RG Jr, **Murphy BR**. Resistance to challenge with influenza A/Hong Kong/123/77 (H1N1) wild type virus induced by live attenuated A/Hong Kong/123/77 (H1N1) cold-adapted reassortant virus. *J Infect Dis* 1985;151:744-745.
112. Brown TA, **Murphy BR**, Radl J, Haaijman JJ, Mestecky J. Subclass distribution and molecular form of immunoglobulin A hemagglutinin antibodies in sera and nasal secretions after experimental secondary infection with influenza A virus in humans. *J Clin Microbiol* 1985;22:259-264.
113. Buckler-White A, Naeve CW, **Murphy BR**. Characterization of the genes involved in host-range restriction of avian influenza-A viruses in primates. Cold Spring Harbor Conference 1984. In Lerner R, Brown F, Chanock RM, eds. *Vaccines 85: Modern Approaches to Vaccines: Molecular and Chemical Basis of Resistance to Viral, Bacterial, and Parasitic Diseases*. New York: Cold Spring Harbor Laboratory 1985;345-350.
114. Burlington DB, Wright PF, van Wyke KL, Phelan MA, Mayner RE, **Murphy BR**. Development of subtype-specific and heterosubtypic antibodies to the influenza A virus hemagglutinin following primary infection in children. *J Clin Microbiol* 1985;21:847-849.
115. Chanock RM, **Murphy BR**. Human host responses to genetically altered viruses. In Fields B, Martin MA, Kamely D, eds. *Genetically Altered Viruses in the Environment*. Banbury Conference on Genetically Altered Viruses in the Environment. New York: Cold Spring Harbor Laboratory 1985;265-287.
116. Clements ML, Tierney EL, **Murphy BR**. Response of seronegative and seropositive adult volunteers to live attenuated cold-adapted reassortant influenza A virus vaccine. *J Clin Microbiol* 1985;21:997-999.
117. Coelingh KLV, Winter C, **Murphy BR**. Antigenic variation in the hemagglutinin-neuraminidase protein of human parainfluenza type 3 virus. *Virology* 1985;143:569-582.
118. Hemming VG, Prince GA, Horswood RL, London WT, **Murphy BR**, Walsh EE, Fischer GW, Weisman LE, Baron PA, Chanock RM. Studies of passive immunity for infections of respiratory syncytial virus in the respiratory tract of a primate model. *J Infect Dis* 1985;152:1083-1086.
119. **Murphy BR**, Chanock RM. Immunization against viruses. In Fields B, *et al.* eds. *Virology*. New York: Raven Press 1985;349-370.
120. **Murphy BR**, Webster RG. Influenza viruses. In Fields B, *et al.*, eds. *Virology*. New York: Raven Press 1985;1179-1239.
121. **Murphy BR**, Clements ML, Tierney EL, Black RE, Steinberg J, Chanock RM. Dose response of influenza A/Washington/897/80 (H3N2) avian-human reassortant virus in adult volunteers. *J Infect Dis* 1985;152:225-229.

122. Snyder MH, Clements ML, DeBorde D, Maassab HF, **Murphy BR**. Attenuation of wild-type influenza A virus by acquisition of the PA polymerase and matrix protein genes of the influenza A/Ann Arbor/6/60 cold-adapted donor virus. *J Clin Microbiol* 1985;22:719-725.
123. Tian S-F, Buckler-White AJ, London WT, Reck L, Chanock RM, **Murphy BR**. Nucleoprotein and membrane protein genes are associated with restriction of replication of influenza A/Mallard/NY/78 virus and its reassortants in squirrel monkey respiratory tract. *J Virol* 1985;53:771-775.
124. Tian S-F, **Murphy BR**. The hemagglutinin of influenza A/Fuzhou/8/58 (H2N2) virus affects replication in the nasal turbinates of hamsters. *Chinese J Virol* 1985;1:133-140.
125. Van Voris L, Betts RF, Menegus M, **Murphy BR**, Roth FK, Douglas RGJr. Serological diagnosis of influenza A/USSR/77 H1N1 infection: value of ELISA compared to other antibody techniques. *J Med Virol* 1985;16:315-320.
126. Buckler-White AJ, **Murphy BR**. Nucleotide sequence analysis of the nucleoprotein gene of an avian and a human influenza virus strain identifies two classes of nucleoproteins. *Virology* 1986;155:345-355.
127. Buckler-White AJ, Naeve CW, **Murphy BR**. Characterization of a gene coding for M proteins which is involved in host range restriction of an avian influenza A virus in monkeys. *J Virol* 1986;57:697-700.
128. Clements ML, Betts RF, Tierney EL, **Murphy BR**. Comparison of inactivated and live influenza A virus vaccines. In Kendal AP, Patriarca PA, eds. *Options for the Control of Influenza*. New York: Alan R. Liss 1986;255-269.
129. Clements ML, Betts RF, Tierney EL, **Murphy BR**. Resistance of adults to challenge with influenza A wild-type virus after receiving live or inactivated virus vaccine. *J Clin Microbiol* 1986;23:73-76.
130. Clements ML, Betts RF, Tierney EL, **Murphy BR**. Serum and nasal wash antibodies associated with resistance to experimental challenge with influenza A wild-type virus. *J Clin Microbiol* 1986;24:157-160.
131. Clements ML, **Murphy BR**. Development and persistence of local and systemic antibody responses in adults given live attenuated or inactivated influenza A virus vaccine. *J Clin Microbiol* 1986;23:66-72.
132. Clements ML, Snyder MH, Buckler-White AJ, Tierney EL, London WT, **Murphy BR**. Evaluation of avian-human reassortant influenza A/Washington/897/80 x A/Pintail/119/79 virus in monkeys and adult-volunteers. *J Clin Microbiol* 1986;24:47-51.
133. Coelingh KL, Winter CC, **Murphy BR**, Ricé JM, Kimball PC, Collins PL. Conserved epitopes on the hemagglutinin-neuraminidase proteins of human and bovine

parainfluenza type 3 viruses: nucleotide sequence analysis of variants selected with monoclonal antibodies. *J Virol* 1986;60:90-96.

134. Elango N, Prince GA, **Murphy BR**, Venkatesan S, Chanock RM, Moss B. Resistance to human respiratory syncytial virus (RSV) infection induced by immunization of cotton rats with a recombinant vaccinia virus expressing the RSV G glycoprotein. *Proc Natl Acad Sci USA* 1986;83:1906-1910.
135. **Murphy BR**, Alling D, Snyder MH, Walsh EE, Prince GA, Chanock RM, Hemming VG, Rodriguez WJ, Kim HW, Graham BS, Wright PF. The effect of age and preexisting antibody response of infants and children to the F and G glycoproteins during respiratory syncytial virus infection. *J Clin Microbiol* 1986;24:894-898.
136. **Murphy BR**, Graham BS, Prince GA, Walsh EE, Chanock RM, Karzon DT, Wright PF. Serum and nasal-wash immunoglobulin G and A antibody response of infants and children to respiratory syncytial virus F and G glycoproteins following primary infection. *J Clin Microbiol* 1986;23:1009-1014.
137. **Murphy BR**, Prince GA, Walsh EE, Kim HW, Hemming VG, Rodriguez W, Chanock RM. Dissociation between serum neutralizing and glycoprotein antibody responses of infants and children who received inactivated respiratory syncytial virus vaccine. *J Clin Microbiol* 1986;24:197-202.
138. Olmsted RA, Elango N, Prince GA, **Murphy BR**, Johnson PR, Moss B, Chanock RM, Collins PL. Expression of the F glycoprotein of respiratory syncytial virus by a recombinant vaccinia virus: comparison of the individual contributions of the F and G glycoproteins to host immunity. *Proc Natl Acad Sci USA* 1986;83:7462-7466.
139. Prince GA, Jenson AB, Hemming VG, **Murphy BR**, Walsh EE, Horswood RL, Chanock RM. Enhancement of respiratory syncytial virus pulmonary pathology in cotton rats by prior intramuscular inoculation of formalin-inactivated virus. *J Virol* 1986;57:721-728.
140. Prince GA, **Murphy BR**, Chanock RM, Hemming VG, Walsh EE. Mechanism by which intramuscular inoculation of formalin-inactivated respiratory syncytial virus (RSV) enhances pulmonary pathology in cotton rats subsequently infected with RS virus. In Brown F, Chanock RM, Lerner RA, eds. *Vaccines 86: New Approaches to Immunization*. New York: Cold Spring Harbor 1986;261-266.
141. Smith GL, Bennink JR, Yewdell JW, Small PA Jr, **Murphy BR**, Moss B. Vaccinia virus recombinants expressing influenza virus genes. Proceedings Viratek-UCLA Symposia on Molecular and Cellular Biology, Keystone, Colorado, April 20-25, 1985. In Kendal AP, Patriarca, PA, eds. *Options for the Control of Influenza*. New York: Alan R. Liss 1986;375-389.
142. Snyder MH, Clements ML, Betts RF, Dolin R, Buckler-White AJ, Tierney EL, **Murphy BR**. Evaluation of live avian-human reassortant influenza A H3N2 and H1N1 virus vaccines in seronegative adult volunteers. *J Clin Microbiol* 1986;23:852-857.

143. Snyder MH, Clements ML, Herrington D, London WT, Tierney EL, **Murphy BR**. Comparison by studies in squirrel monkeys, chimpanzees, and adult humans of avian-human influenza A virus reassortants derived from different avian influenza virus donors. *J Clin Microbiol* 1986;23:467-469.
144. Snyder, M.H., W.T. London, E.L. Tierney, H.F. Maassab, and B.R. Murphy. Restricted replication of a cold adapted (*ca*) reassortant influenza virus in the lower respiratory tract of chimpanzees. *J Infect Dis* 1986;154:370-371.
145. Snyder MH, Stephenson EH, Young H, York CG, Tierney EL, London WT, Chanock RM, **Murphy BR**. Infectivity and antigenicity of live avian-human influenza A reassortant virus: comparison of intranasal and aerosol routes in squirrel monkeys. *J Infect Dis* 1986;154:709-712.
146. Wagner DK, Graham BS, Wright PF, Walsh EE, Kim HW, Reimer CB, Nelson DL, Chanock RM, **Murphy BR**. The serum immunoglobulin G antibody subclass responses to respiratory syncytial virus F and G glycoproteins following primary infection. *J Clin Microbiol* 1986;24:304-306.
147. Brown TA, Clements ML, **Murphy BR**, Radl J, Haaijman JJ, Mestecky J. Molecular form and subclass distribution of IgA antibodies after immunization with live and inactivated influenza A vaccines. In Mestecky J, McGhee JR, Bienstock J, Orga PL, eds. *Recent Advances in Mucosal Immunology Part B*. New York: Plenum Publishing Corporation 1987;1691-1700.
148. Coelingh KWW, Rice JM, Kimball PC, Winter CC, **Murphy BR**, Collins PL. Hemagglutinin-neuraminidase protein epitopes shared by human and bovine parainfluenza type 3 viruses: nucleotide sequence analysis of variants selected with monoclonal antibodies. In Mahy B, Kolakofsky D, eds. *The Biology of Negative Strand Viruses*. Chapter 52. Amsterdam: Elsevier 1987;391-396.
149. Coelingh KWW, Winter CC, Jorgensen ED, **Murphy BR**. Antigenic and structural properties of the hemagglutinin-neuraminidase glycoprotein of human parainfluenza type 3: sequence analysis of variants selected with monoclonal antibodies which inhibit infectivity, hemagglutination, and neuraminidase activities. *J Virol* 1987;61:1473-1477.
150. Coelingh KWW, Winter CC, **Murphy BR**. Antigenic relationships between the hemagglutinin-neuraminidase glycoproteins of human and bovine type 3 parainfluenza viruses. In Chanock RM, Lerner RA, Brown F, Ginsberg H, eds. *Vaccines 87: Modern Approaches to New Vaccines Including Prevention of AIDS and Other Viral, Bacterial, and Parasitic Diseases*. New York: Cold Spring Harbor Laboratory 1987;296-301.
151. Coelingh KWW, **Murphy BR**, Collins PL, Lebacq-Verheyden AM, Battey JF. Expression of biologically active and antigenically authentic parainfluenza type 3 hemagglutinin-neuraminidase glycoprotein by a recombinant baculovirus. *Virology* 1987;160:465-472.
152. Johnson PR, Olmsted RA, Prince GA, **Murphy BR**, Alling DW, Walsh EE, Collins PL. Antigenic relatedness between the glycoproteins of human respiratory syncytial virus

subgroups A and B: Evaluation of the contributions of the F and G glycoproteins to immunity. *J Virol* 1987;61:3163-3166.

153. Maassab HF, Snyder MH, Odagiri T, Donabedian AM, Deborde DC, **Murphy BR**. The role of specific genes from cold-adapted A and B "master" strains in conferring phenotypic and genetic markers of attenuation to candidate vaccine reassortants. In Mahy B, Kolskofsky D, eds. *The Biology of Negative Strand Viruses*. Chapter 45. Amsterdam: Elsevier 1987;341-348.
154. **Murphy BR**, Snyder MH, Buckler-White AJ, Clements ML, Betts BF, London WT, Chanock RM. Avian-human influenza A virus reassortants as live virus vaccines in humans. In Mahy B, Kolakofsky D, eds. *The Biology of Negative Strand Viruses*. Amsterdam: Elsevier 1987;404-411.
155. Flexner C, **Murphy BR**, Rooney J, Wohlenberg C, Yuferov V, Notkins A, Moss B. Successful vaccination with a polyvalent live vector despite immunity to expressed antigens. *Nature (London)* 1988;335:259-262.
156. **Murphy BR**, Prince G, Wagner DK, Walsh EE, Chanock RM. The immune response of humans and cotton rats to respiratory syncytial virus (RSV) infection or formalin-inactivated vaccine. In Chanock RM, Lerner RA, Brown F, Ginsberg H, eds. *Vaccines 87: Modern Approaches to New Vaccines Including Prevention of AIDS and Other Viral, Bacterial, and Parasitic Diseases*. New York: Cold Spring Harbor Laboratory 1987;290-295.
157. Olmsted RA, Johnson PR, Prince GA, **Murphy BR**, Moss B, Chanock RM, Collins PL, Elango N. Immunogenicity and protective efficacy of a recombinant vaccinia virus expressing the F glycoprotein of respiratory syncytial virus. In Chanock RM, Lerner RA, Brown F, Ginsberg H, eds. *Vaccines 87: Modern Approaches to New Vaccines Including Prevention of AIDS and Other Viral, Bacterial, and Parasitic Diseases*. New York: Cold Spring Harbor Laboratory 1987;350-355.
158. Patterson RG, Lamb RA, Moss B, **Murphy BR**. Comparison of the relative roles of the F and HN surface glycoproteins of the paramyxovirus simian virus 5 in inducing protective immunity. *J Virol* 1987;61:1972-1977.
159. Snyder MH, Buckler-White AJ, London WT, Tierney EL, **Murphy BR**. The avian influenza virus nucleoprotein gene and a specific constellation of avian and human virus polymerase genes each specify attenuation of avian-human influenza A/Pintail/79 reassortant viruses for monkeys. *J Virol* 1987;61:2857-2863.
160. Spriggs M, **Murphy BR**, Prince GA, Olmsted RA, Collins PL. Expression of the F and HN glycoproteins of human parainfluenza virus type 3 by recombinant vaccinia viruses: contributions of the individual proteins to host immunity. *J Virol* 1987;61:3416-3423.
161. Wagner DK, Nelson DL, Walsh EE, Reimer CB, Henderson FW, **Murphy BR**. Differential immunoglobulin G subclass antibody titers to respiratory syncytial virus F and G glycoproteins in adults. *J Clin Microbiol* 1987;25:748-750.

162. Wagner DK, Clements ML, Reimer CB, Snyder MH, Nelson DL, **Murphy BR**. Analysis of IgG antibody responses after live and inactivated influenza A vaccine indicate that nasal wash IgG is a transudate from serum. *J Clin Microbiol* 1987;25:559-562.
163. Betts RF, Douglas RGJr, Maassab HF, DeBorde DC, Clements ML, **Murphy BR**. Analysis of virus and host factors in a study of A/Peking/2/79 (H3N2), cold adapted vaccine recombinant in which vaccine associated illness occurred in normal volunteers. *J Med Virol* 1988;26:175-183.
164. Chanock RM, **Murphy BR**, Collins PL, Coelingh KVW, Olmsted RA, Snyder MH, Spriggs MK, Prince GA, Moss B, Flores J, Gorziglia M, Kapikian AZ. Live viral vaccines for respiratory and enteric tract diseases. *Vaccine* 1988;6:129-133.
165. Coelingh KLV, Winter CC, Tierney EL, London WT, **Murphy BR**. Attenuation of bovine parainfluenza virus type 3 in non-human primates and its ability to confer immunity to human parainfluenza virus type 3 challenge. *J Infect Dis* 1988;157:655-662.
166. Coelingh KVW, Winter CC, **Murphy BR**. Nucleotide and deduced amino acid sequence of hemagglutinin-neuraminidase genes of human type 3 parainfluenza viruses isolated from 1957-1983. *Virology* 1988;162:137-143.
167. Coelingh K, Battey J, Lebacq-Verheyden A, Collins P, Murphy B. Development of live virus and subunit vaccines for parainfluenza type 3 virus. In Chanock RM, Lerner RA, Brown F, Ginsberg H, eds. *Modern Approaches to New Vaccines Including Prevention of AIDS*. New York: Cold Spring Harbor Laboratory 1988;171-177.
168. Flexner C, **Murphy BR**, Rooney J, Wohlenberg C, Yuferov V, Notkins A, Moss B. Successful vaccination with a polyvalent live vector despite immunity to expressed antigens. *Nature (London)* 1988;335:259-262.
169. Hendry RM, Burns JC, Walsh EE, Graham BS, Wright PF, Hemming VG, Rodriguez WJ, Kim HW, Prince GA, McIntosh K, Chanock RM, **Murphy BR**. Strain-specific serum antibody responses in infants undergoing primary infection with respiratory syncytial virus. *J Infect Dis* 1988;157:640-647.
170. **Murphy BR**, Clements ML, Johnson PR, Wright PF. The mucosal and systemic immune responses of children and adults to live and inactivated influenza A virus vaccines. In Strober W, Lamm M, McGhee J, James S, eds. *Mucosal Immunity and Infection at Mucosal Surfaces*. Oxford University Press 1988;303-318.
171. **Murphy BR**, Walsh EE. Formalin-inactivated respiratory syncytial virus vaccine induces antibodies to the fusion glycoprotein that are deficient in fusion-inhibiting activity. *J Clin Microbiol* 1988;26:1595-1597.
172. **Murphy BR**, Prince GA, Collins PL, Coelingh KVW, Olmsted RA, Spriggs MK, Parrott RH, Kim H-W, Brandt CD, Chanock RM. Current approaches to the development of vaccines effective against parainfluenza and respiratory syncytial viruses. *Virus Res* 1988;11:1-15.

173. Murphy BR, Olmsted RA, Collins PL, Chanock RM, Prince GA. Passive transfer of respiratory syncytial virus (RSV) immune serum suppresses the immune response to the RSV fusion (F) and large (G) glycoproteins expressed by recombinant vaccinia viruses. *J Virol* 1988;62:3907-3910.
174. Murphy BR. Current approaches to the development of vaccines effective against parainfluenza viruses. *Bull WHO* 1988;66:391-397.
175. Olmsted RA, Buller RML, Murphy BR, London WT, Beeler JA, Collins PL. Evaluation in non-human primates of the safety, immunogenicity and efficacy of recombinant vaccinia viruses expressing the F and G glycoproteins of respiratory syncytial virus. In Chanock RM, Lerner RA, Brown F, Ginsberg H, eds. *Modern Approaches to New Vaccines Including Prevention of AIDS*. New York: Cold Spring Harbor Laboratory 1988;205-210.
176. Olmsted RA, Buller RML, Collins PL, London WT, Beeler JA, Prince GA, Chanock RM, Murphy BR. Evaluation in non-human primates of recombinant vaccinia viruses expressing the F or G Glycoproteins of respiratory syncytial virus. *Vaccine* 1988;6:519-524.
177. Prince GA, Hemming VG, Murphy BR, Chanock RM. The prophylactic and therapeutic effect of serum antibody on respiratory syncytial virus infection of laboratory animals. In Strober W, Lamm M, McGhee J, James S, eds. *Mucosal Immunity and Infection at Mucosal Surfaces*. Oxford University Press 1988;279-283.
178. Sears SD, Clements ML, Betts RF, Maassab HF, Murphy BR, Snyder MH. Comparison of live attenuated H1N1 and H3N2 cold-adapted and avian-human influenza A reassortant viruses and inactivated virus vaccine in adults. *J Infect Dis* 1988;158:1209-1219.
179. Snyder MH, Betts RF, DeBorde D, Tierney EL, Clements ML, Harrington D, Sears SD, Dolin R, Maassab HF, Murphy BR. Four viral genes independently contribute to attenuation of live influenza A/Ann Arbor/6/60 (H2N2) cold-adapted reassortant virus vaccines. *J Virol* 1988;62:488-495.
180. Snyder MH, Betts RF, Clements ML, Harrington D, Sears SD, Maassab HF, Murphy BR. Identification of four genes which attenuate influenza A/Ann Arbor/6/60 (H2N2) cold-adapted reassortant viruses. In Chanock RM, Lerner RA, Brown F, Ginsberg H, eds. *Modern Approaches to New Vaccines Including Prevention of AIDS*. New York: Cold Spring Harbor Laboratory 1988;145-149.
181. Snyder MH, Banks S, Murphy BR. Determination of antibody response to influenza virus surface glycoprotein by kinetic enzyme-linked immunosorbent assay. *J Clin Microbiol* 1988;26:2034-2040.
182. Spriggs MK, Collins PL, Tierney EL, London WT, Murphy BR. Immunization with vaccinia virus recombinants that express the surface glycoproteins of human parainfluenza virus type 3 (PIV3) protects patas monkeys against PIV3 infection. *J Virol* 1988;62:1293-1296.

183. Yarchoan R, Strober W, **Murphy BR**, Nelson DL. *In vitro* production of IgA antibody by human lymphocytes. In Strober W, Lamm M, McGhee J, James S, eds. *Mucosal Immunity and Infection at Mucosal Surfaces*. Oxford University Press 1988;94-103.
184. Vasantha S, Coelingh KVV, **Murphy BR**, Dourmashkin RR, Hammer CH, Frank MM, Fries LF. Interactions of a non-neutralizing IgM antibody and complement in parainfluenza virus neutralization. *Virology* 1988;167:433-441.
185. Chanock RM, McIntosh K, **Murphy BR**, Parrott RH. Respiratory syncytial virus. In Evans AS, ed. *Viral Infections of Humans: Epidemiology and Control*, 3rd ed. New York: Plenum Publishing Corporation 1989;525-244.
186. Clements ML, Sears SD, Christina K, **Murphy BR**, Snyder MH. Comparison of the virologic and immunologic responses of volunteers to live avian-human influenza A H3N2 reassortant virus vaccines derived from two different avian influenza virus donors. *J Clin Microbiol* 1989;27:219-222.
187. **Murphy BR**. Summary. In Chanock RM, Lerner RA, Brown F, Ginsberg H, eds. *Vaccines 89: Modern Approaches to New Vaccines Including Prevention of AIDS*. New York: Cold Spring Harbor Laboratory 1989;535-542.
188. **Murphy BR**, Olmsted RA, Collins PL, Chanock RM, Prince GA. Intranasal immunization with vaccinia-RS recombinant-viruses is superior to intradermal immunization in animals with passively acquired RS virus antibodies. In Chanock RM, Lerner RA, Brown F, Ginsberg H, eds. *Vaccines 89: Modern Approaches to New Vaccines Including Prevention of AIDS*. New York: Cold Spring Harbor Laboratory 1989;501-505.
189. **Murphy BR**, Clements ML. The systemic and mucosal immune response of humans to influenza A virus. In Mestecky J, McGhee JR, eds. *Current Topics in Microbiology and Immunology*, vol. 146. International Symposium on New Strategies for Oral Immunization, 1988. Heidelberg: Springer-Verlag 1989;123-136.
190. **Murphy BR**, Collins PL, Lawrence L, Zubak J, Chanock RM, Prince GA. Immuno-suppression of the antibody response to respiratory syncytial virus (RSV) by pre-existing serum antibodies: partial abrogation by topical infection of the respiratory tract with vaccinia virus-RSV recombinants. *J Gen Virol* 1989;70:2185-2190.
191. **Murphy BR**, Buckler-White AJ, London WT, Snyder MH. Characterization of the M protein and nucleoprotein genes of an avian influenza A virus which are involved in host range restriction in monkeys. *Vaccine* 1989;7:557-561.
192. **Murphy BR**, Paradiso PR, Hildreth S, Hockmeyer WT, Jensen AB, Sotnikov A, Lawrence L, Zubak JJ, Chanock RM, Prince GA. Immunization of cotton rats with the fusion (F) and large (G) glycoproteins of respiratory syncytial virus (RSV) protects against RSV challenge without potentiating RSV disease. *Vaccine* 1989;7:533-540.

193. Olmsted RA, **Murphy BR**, Lawrence LA, Elango N, Moss B, Collins PL. Processing, surface expression, and immunogenicity of carboxy-terminally truncated mutants of G protein of human respiratory syncytial virus. *J Virol* 1989;63:411-420.
194. Powers DC, Sears SD, **Murphy BR**, Thumar B, Clements ML. Systemic and local antibody responses in elderly subjects given live or inactivated influenza A virus vaccines. *J Clin Microbiol* 1989;27:2666-2671.
195. Snyder MH, London WT, Maassab HF, **Murphy BR**. Attenuation and phenotypic stability of influenza B/Texas/84 cold-adapted reassortant virus: studies in hamsters and chimpanzees. *J Infect Dis* 1989;160:604-610.
196. Treanor J, Snyder MH, London WT, **Murphy BR**. The B allele of the NS gene of avian influenza viruses, but not the A allele, attenuates human influenza A virus for squirrel monkeys. *Virology* 1989;171:1-9.
197. Treanor J, Kawaoka Y, Miller R, **Murphy BR**. Nucleotide sequence of the avian influenza A/Mallard/NY/6750/78 polymerase genes. *Virus Res* 1989;14:257-270.
198. Wagner DK, Muelenaer P, Henderson FW, Snyder M, Reimer CB, Walsh EE, Nelson D, **Murphy BR**. Serum immunoglobulin G antibody subclass response to respiratory syncytial virus F and G glycoproteins after first, second and third infections. *J Clin Microbiol* 1989;27:589-592.
199. Wathen MW, Brideau RJ, Thomsen DR, Stier MA, **Murphy BR**. Characterization of a novel human respiratory syncytial virus chimeric FG glycoprotein expressed with a baculovirus vector. *J Gen Virol* 1989;70:2625-2635.
200. Clements ML, Snyder MH, Sears SD, Maassab HF, **Murphy BR**. Evaluation of the infectivity, immunogenicity and efficacy of live cold-adapted influenza B/Ann Arbor/86 reassortant virus vaccine in adult volunteers. *J Infect Dis* 1990;161:869-877.
201. Coelingh KLVW, Winter CC, Tierney EL, Hall SL, London WT, Kim H-W, Chanock RM, **Murphy BR**. Antibody responses of humans and nonhuman primates to individual antigenic sites of the hemagglutinin-neuraminidase and fusion glycoproteins after primary infection or reinfection with parainfluenza type 3 virus. *J Virol* 1990;64:3833-3843.
202. Collins PL, Purcell RH, London WT, Lawrence LA, Chanock RM, **Murphy BR**. Evaluation in chimpanzees of vaccinia virus recombinants that express the surface glycoproteins of human respiratory syncytial virus. *Vaccine* 1990;8:164-168.
203. Collins PL, Davis AR, Lubeck MD, Mizutani S, Hung PP, Prince GA, Purcell RH, Chanock RM, **Murphy BR**. Evaluation of the protective efficacy of recombinant vaccinia viruses and adenoviruses that express respiratory syncytial virus glycoproteins. In Brown F, Chanock RM, Ginsberg H, Lerner RA, eds. *Vaccines 90: Modern Approaches to New Vaccines Including Prevention of AIDS*. Cold Spring Harbor, NY: Cold Spring Harbor Laboratory 1990;79-84.

204. Flexner C, Moss B, London WT, **Murphy BR**. Attenuation and immunogenicity in primates of vaccinia virus recombinants expressing human interleukin-2. *Vaccine* 1990;8:17-21.
205. **Murphy BR**, Chanock RM. Immunization against viruses. In Fields BN, Knipe DM, Chanock RM, Hirsch MS, Melnick JL, Monath TP, eds. *Virology*, 2nd ed. New York: Raven Press 1990;469-502.
206. **Murphy BR**, Webster RG. Orthomyxoviruses. In Fields BN, Knipe DM, Chanock RM, Hirsch MS, Melnick JL, Monath TP, eds. *Virology*, 2nd ed. New York: Raven Press 1990;1091-1152.
207. **Murphy BR**, Tierney EL, London WT, Belshe RB. A cold-adapted mutant of human parainfluenza virus type 3 is attenuated and protective in chimpanzees. In Brown F, Chanock RM, Ginsberg HS, Lerner RA, eds. *Vaccines 90: Modern Approaches to New Vaccines Including Prevention of AIDS*. Cold Spring Harbor, NY: Cold Spring Harbor Laboratory 1990;91-95.
208. **Murphy BR**, Prince GA, Lawrence L, Croen K, Collins P. Detection of respiratory syncytial virus (RSV) infected cells by *in situ* hybridization in the lungs of cotton rats immunized with formalin-inactivated virus or purified RSV F and G glycoprotein subunit vaccine and challenged with RSV. *Virus Res* 1990;16:153-162.
209. **Murphy BR**, Sotnikov A, Lawrence L, Banks S, Alling D, Prince G. Enhanced pulmonary histopathology is observed in cotton rats immunized with formalin-inactivated respiratory syncytial virus (RSV) or purified F glycoprotein and challenged with RSV 3-6 months after immunization. *Vaccine* 1990;8:497-502.
210. Prince GA, Hemming VG, Horswood RL, Baron PA, **Murphy BR**, Chanock RM. Mechanism of antibody-mediated viral clearance in immunotherapy of respiratory syncytial virus infection of cotton rats. *J Virol* 1990;64:3091-3092.
211. Snyder MH, London WT, Maassab HF, Chanock RM, **Murphy BR**. A 36 nucleotide deletion mutation in the coding region of the NS1 gene of an influenza A virus RNA segment 8 specifies a temperature-dependent host range phenotype. *Virus Res* 1990;15:69-84.
212. Steinhoff MD, Halsey NA, Wilson MH, Burns BA, Samorodin RK, Fries LF, **Murphy BR**, Clements ML. Comparison of live attenuated cold-adapted and avian-human influenza A/Bethesda/85 (H3N2) reassortant virus vaccines in infants and children. *J Infect Dis* 1990;162:394-401.
213. Treanor JJ, Tierney EL, Zebedee SL, Lamb RA, **Murphy BR**. Passively transferred monoclonal antibody to the M2 protein inhibits influenza A virus replication in mice. *J Virol* 1990;64:1375-1377.
214. Treanor J, **Murphy BR**. Genes involved in the restriction of replication of avian influenza A viruses in primates. In Kurstak E, Marusyk RG, Murphy FA, Van

Regenmortel MHV, eds. *Applied Virology Research: Virus Variation and Epidemiology*, Vol. 2. New York: Plenum Publishing Corporation 1990;150-176.

215. Chanock RM, **Murphy BR**. Past efforts to develop safe and effective RSV vaccines. In Meignier B, *et al.*, eds. *Animal Models of Respiratory Syncytial Virus Infections*. Merieux Foundation Publication 1991:35-42.
216. Clements ML, Belshe RB, King J, Newman F, Westblom TU, Tierney EL, London WT, **Murphy BR**. Evaluation of bovine, cold-adapted human, and wild-type human parainfluenza type 3 viruses in adults and chimpanzees. *J Clin Microbiol* 1991;**29**:1175-1182.
217. Collins PL, Connors M, Chanock RM, **Murphy BR**. Expression of respiratory syncytial virus genes by recombinant expression vectors. In Meignier B, *et al.*, eds. *Animal Models of Respiratory Syncytial Virus Infections*. Merieux Foundation Publication 1991;137-146.
218. Connors M, Collins PL, Firestone C-Y, **Murphy BR**. The role of individual RSV proteins in resistance to infection. In Meignier B, *et al.*, eds. *Animal Models of Respiratory Syncytial Virus Infections*. Merieux Foundation Publication 1991;53-56.
219. Connors M, Collins PL, Firestone C-Y, **Murphy BR**. Respiratory syncytial virus F, G, M2 (22K) and N proteins each induce resistance to RSV challenge, but the resistance induced by the M2 and N proteins is relatively short-lived. *J Virol* 1991;**65**:1634-1637.
220. Connors M, Collins PL, Firestone C-Y, **Murphy BR**. Respiratory syncytial virus F, G, M2 (22K), and N proteins each induce resistance to RSV challenge, but the resistance induced by the M2 and N proteins is relatively short-lived. In Chanock RM, Ginsberg HS, Brown F, Lerner RA, EDS. *Vaccines 91: Modern Approaches to New Vaccines Including Prevention of AIDS*. Cold Spring Harbor: Cold Spring Harbor Laboratory Press 1991;277-281.
221. Edwards KM, King JC, Steinhoff MC, Thompson J, Clements ML, Wright PF, **Murphy BR**. Safety and immunogenicity of live attenuated cold-adapted influenza B/Ann Arbor/1/86 reassortant virus vaccine in infants and children. *J Infect Dis* 1991;**163**:740-745.
222. Hall SL, **Murphy BR**, Coelingh KLVW. Protection of cotton rats by immunization with the human parainfluenza virus type 3 fusion (F) glycoprotein expressed on the surface of insect cells infected with a recombinant baculovirus. *Vaccine* 1991;**9**:659-667.
223. Hsu K-H, Lubeck MD, Davis AR, Bhat RA, Selling BH, Bhat BM, Mizutani S, Hung PP, **Murphy BR**, Collins PL, Chanock RM. Immunogenicity and protective efficacy of adenovirus vectored respiratory syncytial virus vaccine. In Chanock RM, Ginsberg HS, Brown F, Lerner RA, eds. *Vaccines 91: Modern Approaches to New Vaccines Including Prevention of AIDS*. Cold Spring Harbor: Cold Spring Harbor Laboratory Press 1991;293-297.

224. Kanesaki T, **Murphy BR**, Collins PL, Ogra PL. Effectiveness of enteric immunization in the development of secretory IgA response and the outcome of infection with respiratory syncytial virus. *J Virol* 1991;65:657-663.

225. Muelenaer PM, Henderson FW, Hemming VG, Walsh EE, Anderson LJ, Prince GA, **Murphy BR**. Group-specific serum antibody responses in children with primary and recurrent respiratory syncytial virus infections. *J Infect Dis* 1991;164:15-21.

226. **Murphy BR**, Prince GA, Collins PL, Hildreth SW, Paradiso PR. Effect of passive antibody on the immune response of cotton rats to purified F and G glycoproteins of respiratory syncytial virus (RSV). *Vaccine* 1991;9:185-189.

227. Murphy, BR, Steinhoff MC, Fries LF, Halsey NA, Wilson MH, King J, Clements ML. Surface glycoproteins from a wild-type influenza-A parent virus modify the infectivity and virulence of live attenuated influenza-A avian-human reassortant viruses for seronegative humans. In Chanock RM, Ginsberg HS, Brown F, Lerner RA, eds. *Vaccines 91: Modern Approaches to New Vaccines Including Prevention of AIDS*. Cold Spring Harbor: Cold Spring Harbor Laboratory Press 1991;203-207.

228. **Murphy BR**. Parainfluenza viruses. In Gorbach S, Bartlett J, Blacklow N, eds. *Infectious Diseases*. Philadelphia: WB Saunders 1991;1745-1751.

229. **Murphy BR**, Chanock RM. The immunobiology of RSV. In Meignier B, *et al.*, eds. *Animal Models of Respiratory Syncytial Virus Infections*. Merieux Foundation Publication 1991;25-30.

230. **Murphy BR**, Connors M. Immunization of cotton rats with formalin-inactivated RSV or RSV subunit vaccine results in enhanced pulmonary histopathology following RSV challenge. In Meignier B, *et al.*, eds. *Animal Models of Respiratory Syncytial Virus Infections*. Merieux Foundation Publication 1991;81-86.

231. Muster T, Subbarao EK, Enami M, **Murphy BR**, Palese P. An influenza A virus containing influenza B virus 5' and 3' noncoding regions on the neuraminidase gene is attenuated in mice. *Proc Natl Acad Sci USA* 1991;88:5177-5181.

232. Powers DC, Fries LF, **Murphy BR**, Thumar B, Clements ML. In elderly persons live attenuated influenza A virus vaccines do not offer an advantage over inactivated virus vaccine in inducing serum or secretory antibodies or local immunologic memory. *J Clin Microbiol* 1991;29:498-505.

233. Steinhoff MC, Halsey NA, Fries LF, Wilson MH, King J, Burns BA, Samorodin RK, Perkis V, **Murphy BR**, Clements ML. The A/Mallard/6750/78 avian-human, but not the A/Ann Arbor/6/60 cold-adapted, influenza A/Kawasaki/86 (H1N1) reassortant virus vaccine retains partial virulence for infants and children. *J Infect Dis* 1991;165:1023-1028.

234. Treanor JJ, Tierney EL, London WT, **Murphy BR**. Characterization of the attenuating M and NP gene segments of the avian influenza A/Mallard/78 virus during *in vitro*

production of avian-human reassortant vaccine viruses and after replication in humans and primates. *Vaccine* 1991;9:495-501.

235. Treanor JT, Buja R, **Murphy BR**. Intragenic suppression of a deletion mutation of the nonstructural gene of an influenza A virus. *J Virol* 1991;65:4204-4210.
236. Belshe RB, Karron RA, Newman FK, Anderson EL, Nugent SL, Steinhoff M, Clements ML, Wilson MH, Hall SL, Tierney EL, **Murphy BR**. Evaluation of a live attenuated cold-adapted parainfluenza virus type 3 vaccine in children. *J Clin Microbiol* 1992;30:2064-2070.
237. Chanock RM, Parrott RH, Connors M, Collins PL, **Murphy BR**. Serious respiratory tract disease caused by respiratory syncytial virus: Prospects for improved therapy and effective immunization. *Pediatrics* 1992;90:137-143.
238. Clements, ML, Subbarao EK, Fries, LF, Karron RA, London WT, **Murphy BR**. Use of single gene reassortant viruses to study the role of avian influenza A virus genes in attenuation of wild-type human influenza A virus for squirrel monkeys and adult volunteers. *J Clin Microbiol* 1992;30:655-662
239. Connors M, Collins PL, Firestone C-Y, Sotnikov AV, Waitze A, Davis AR, Hung PP, Chanock RM, **Murphy BR**. Cotton rats previously immunized with a chimeric RSV FG glycoprotein develop enhanced pulmonary pathology when infected with RSV, a phenomenon not encountered during immunization with vaccinia-RSV recombinants or RSV. *Vaccine* 1992;10:475-484.
240. Connors M, Kulkarni AB, Collins PL, Firestone C-Y, Holmes KL, Morse HC, **Murphy BR**. Resistance to respiratory syncytial virus (RSV) challenge induced by infection with a vaccinia virus recombinant expressing the RSV M2 protein (Vac-M2) is mediated by CD8<sup>+</sup> T cells, while that induced by Vac-F or Vac-G recombinants is mediated by antibodies. *J Virol* 1992;66:1277-1281.
241. Connors M, Kulkarni AB, Firestone C-Y, Holmes KL, Morse HC III, Sotnikov AV, **Murphy BR**. Pulmonary histopathology induced by respiratory syncytial virus (RSV) challenge of formalin-inactivated RSV immunized BALB/c mice is abrogated by depletion of CD4<sup>+</sup> T-cells. *J Virol* 1992;66:7444-7451.
242. Hall SL, Stokes A, Tierney EL, London WT, Belshe RB, Newman FC, **Murphy BR**. Cold-passaged human parainfluenza type 3 viruses contain *ts* and non-*ts* mutations leading to attenuation in rhesus monkeys. *Virus Res* 1992;22:173-184.
243. Hsu K-HL, Lubeck MD, Davis AR, Bhat RA, Selling BH, Bhat BM, Mizutani S, **Murphy BR**, Collins PL, Chanock RM, Hung PP. Immunogenicity of recombinant adenovirus-respiratory syncytial virus using Ad4, Ad5, and Ad7 vectors in dogs and a chimpanzee. *J Infect Dis* 1992;166:769-775.
244. Lawson CM, Subbarao EK, **Murphy BR**. Nucleotide sequence changes in the polymerase basic protein 2 gene of temperature-sensitive mutants of influenza A virus. *Virology* 1992;191:506-510.

245. **Murphy BR**, Hall SL, Crowe J, Collins PL, Subbarao EK, Connors M, London WT, Chanock RM. The use of chimpanzees in respiratory virus research. In Erwin J, Landon JC, eds. *Chimpanzee Conservation and Public Health: Environments for the Future*. 1992;21-28.

246. Powers DC, **Murphy BR**, Fries LF, Adler WH, Clements ML. Reduced infectivity of cold-adapted influenza A H1N1 virus in the elderly: Correlation with serum and local antibodies. *J Am Geriatr Soc* 1992;40:163-167.

247. Subbarao EK, Kawaoka Y, Ryan-Poirier, Clements ML, **Murphy BR**. A comparison of different approaches to measurement of influenza A virus specific hemagglutination-inhibition antibodies in the presence of serum inhibitors. *J Clin Microbiol* 1992;30:996-999.

248. Subbarao EK, Perkins M, Treanor JJ, **Murphy BR**. The attenuation phenotype conferred by the M gene of the influenza A/Ann Arbor/6/60 cold-adapted virus (H2N2) on the A/Korea/82 (H3N2) reassortant virus results from a gene constellation effect. *Virus Res* 1992;25:37-50.

249. Barbas CF III, Crowe JE, Cababa D, Jones TM, Zebedee SL, **Murphy BR**, Chanock RM, Burton DR. Human monoclonal Fab fragments derived from a combinatorial library bind to respiratory syncytial virus F glycoprotein and neutralize infectivity. *Proc Natl Acad Sci USA* 1993;89:10164-10168.

250. Chanock RM, Crowe JE Jr, **Murphy BR**, Burton DR. Human monoclonal antibody Fab fragments cloned from combinatorial libraries: Potential usefulness in prevention and/or treatment of major human viral diseases. *Infect Agents Dis* 1993;2:118-131.

251. Crowe JE Jr, Barbas CF III, Bui P, Cababa D, Jones TM, Zebedee SL, **Murphy BR**, Chanock RM, Burton DR. Human monoclonal Fab fragments derived from a combinatorial library bind to respiratory syncytial virus F glycoprotein and neutralize infectivity. In Brown F, Chanock RM, Ginsberg HS, Lerner RA, eds. *Vaccines 93: Modern Approaches to New Vaccines Including Prevention of AIDS*. Cold Spring Harbor, NY: Cold Spring Harbor Laboratory 1993;7-11.

252. Crowe JE Jr, Collins PL, London WT, Chanock RM, **Murphy BR**. A comparison in chimpanzees of the immunogenicity and efficacy of live attenuated respiratory syncytial virus (RSV) temperature-sensitive mutant vaccines and vaccinia virus recombinants that express the surface glycoproteins of RSV. *Vaccine* 1993;11:1395-1404.

253. de Sierra TM, Kumar ML, Wasser TE, **Murphy BR**, Subbarao EK. Respiratory syncytial virus (RSV)-specific immunoglobulins in preterm infants. *J Pediatr* 1993;122:787-791.

254. Epstein SL, Misplon JA, Lawson CM, Subbarao EK, Connors M, **Murphy BR**.  $\beta 2$ -microglobulin-deficient mice can be protected against influenza A infection by vaccination with vaccinia-influenza recombinants expressing hemagglutinin and neuraminidase. *J Immunol* 1993;150:5484-5493.

255. Hall SL, Sarris CM, Tierney EL, London WT, **Murphy BR**. A cold-adapted mutant of parainfluenza virus type 3 is attenuated and protective in chimpanzees. *J Infect Dis* 1993;167:958-962.
256. Kulkarni AB, Connors M, Firestone C-Y, Morse III HC, **Murphy BR**. On the inclusion of cytotoxic T cell epitopes in the vaccines against viral infections of the respiratory tract. In Brown F, Chanock RM, Ginsberg HS, Lerner RA, eds. *Vaccines 93: Modern Approaches to New Vaccines Including Prevention of AIDS*. Cold Spring Harbor, NY: Cold Spring Harbor Laboratory 1993;337-342.
257. Kulkarni AB, Connors M, Firestone C-Y, Morse III HC, **Murphy BR**. The cytolytic activity of pulmonary CD8<sup>+</sup> lymphocytes induced by infection with a vaccinia virus recombinant expressing the M2 protein of respiratory syncytial virus (RSV) correlates with resistance to RSV infection in mice. *J Virol* 1993;67:1044-1049.
258. Kulkarni AB, Morse HC III, Bennink JR, Yewdell JW, **Murphy BR**. Immunization of mice with vaccinia-M2 recombinant induces epitope-specific and cross-reactive K<sup>d</sup>-restricted CD8<sup>+</sup> cytotoxic T cells. *J Virol* 1993;67:4086-4092.
259. **Murphy BR**. Factors restraining emergence of new influenza viruses. In Morse S, ed. *Emerging Viruses*. New York, NY: Oxford University Press 1993;234-240.
260. **Murphy BR**. Immunogen-induced enhanced pulmonary histopathology in the RSV cotton rat model. *Vaccine* 1993;11:689-691.
261. **Murphy BR**. Mucosal immunity to viruses. In Ogra PL, Mestecky J, Lamm M, Strober W, McGhee J, Bienenstock J, eds. *Mucosal Immunology: Vol. I. Cellular Basis of Mucosal Immunity*. Academic Press, Inc. 1993;333-343.
262. **Murphy BR**. Use of live, attenuated cold-adapted influenza A reassortant virus vaccines in infants, children, young adults, and elderly adults. *Infect Dis Clin Pract* 1993;2:174-181.
263. Steinhoff MC, Fries LF, Karron RA, Clements ML, **Murphy BR**. Effect of heterosubtypic immunity on infection with attenuated influenza A virus vaccines in young children. *J Clin Microbiol* 1993;31:836-838.
264. Stokes A, Tierney EL, **Murphy BR**, Hall SL. The complete nucleotide sequence of the JS strain of human parainfluenza virus type 3: Comparison with the Wash/47885/57 prototype strain. *Virus Res* 1993;25:91-103.
265. Stokes A, Tierney EL, Sarris CM, **Murphy BR**, Hall SL. The complete nucleotide sequence of two cold-adapted, temperature-sensitive attenuated mutant vaccine viruses (cp12 and cp45) derived from the JS strain of human parainfluenza virus type 3 (PIV3). *Virus Res* 1993;30:43-52.

266. Subbarao EK, Kawaoka Y, **Murphy BR**. Rescue of an influenza A virus type type PB2 gene and a mutant derivative bearing a site-specific temperature sensitive and attenuating mutation. *J Virol* 1993;67:7223-7228.
267. Subbarao EK, London W, **Murphy BR**. A single amino acid substitution is responsible for reversion of the host range restriction phenotype of reassortant viruses that derive their PB2 gene from an avian influenza A virus and remaining genes from a human influenza A virus. *J Virol* 1993;67:1761-1764.
268. Subbarao EK, **Murphy BR**. A general overview of viral vaccine development. In Ciardi JE, McGhee R, Keith J, eds. *Genetically Engineered Vaccines: Prospects for Oral Disease Prevention*. A Volume of *Advances in Experimental Medicine and Biology*, Plenum Press 1993;327:51-58.
269. Connors M, Giese NA, Kulkarni AB, Firestone C-Y, Morse HC III, **Murphy BR**. Enhanced pulmonary histopathology induced by respiratory syncytial virus (RSV) challenge of formalin-inactivated RSV immunized BALB/c mice is abrogated by depletion of IL-4 and IL-10. *J Virol* 1994;68:5321-5325.
270. Crowe JE Jr, Bui PT, Davis AR, Hung PP, Chanock RM, **Murphy BR**. A further attenuated derivative of a cold-passaged temperature-sensitive mutant of human respiratory syncytial virus (RSV<sub>cpts</sub>-248) retains immunogenicity and protective efficacy against wild-type challenge in seronegative chimpanzees. *Vaccine* 1994;12:783-790.
271. Crowe JE Jr, Bui PT, London WT, Davis AR, Hung PP, Chanock RM, **Murphy BR**. Satisfactorily attenuated and protective mutants derived from a partially attenuated cold passaged respiratory syncytial virus mutant by introduction of additional attenuating mutations during chemical mutagenesis. *Vaccine* 1994;12:691-699.
272. Crowe JE Jr., Cheung PYK, Wallace EF, Chanock RM, Lerrick JW, **Murphy BR**, Fry K. Isolation and characterization of a chimpanzee monoclonal antibody to the G-glycoprotein of human respiratory syncytial virus. *Clin Diagn Lab Immunol* 1994;1(6):701-706.
273. Crowe JE Jr, **Murphy BR**, Chanock RM, Williamson A, Barbas CF III, Burton DR. Human RSV monoclonal antibody Fab cloned from a combinatorial library and produced in *E. coli* is effective therapeutically when introduced directly into the lungs of RSV-infected mice. In Brown F, Chanock RM, Ginsberg HS, Norrby E, eds. *Vaccines 94: Modern Approaches to New Vaccines Including Prevention of AIDS*. Cold Spring Harbor: Cold Spring Harbor Laboratory Press 1994;315-320.
274. Crowe JE Jr., **Murphy BR**, Chanock RM, Williamson RA, Barbas CF III, Burton DR. Recombinant human RSV monoclonal antibody Fab is effective therapeutically when introduced directly into the lungs of respiratory syncytial virus-infected mice. *Proc Natl Acad Sci USA* 1994;91:1386-1390.
275. Lawson CM, Bennink JR, Restifo NP, Yewdell JW, **Murphy BR**. Primary pulmonary cytotoxic T lymphocytes induced by immunization with a vaccinia virus recombinant

expressing influenza A virus nucleoprotein peptide do not protect mice against challenge. *J Virol* 1994;68:3505-3511.

276. **Murphy BR**, Crowe JE Jr, Lubeck MD, Hsu K-HL, Hall SL, Karron RA, Clements ML, Wright PF, Belshe RB, Chanock RM. Live attenuated vaccines for respiratory syncytial virus (RSV) and parainfluenza virus type 3 (PIV3). Ross Conference Symposium on Pediatric Vaccines Report 1994;302-313.
277. **Murphy BR**, Hall SL, Kulkarni AB, Crowe JE Jr, Collins PL, Connors M, Karron RA, Chanock RM. An update on approaches to the development of respiratory syncytial virus (RSV) and parainfluenza virus type 3 (PIV3) vaccines. *Virus Res* 1994;32:13-36.
278. **Murphy BR**. Mucosal immunity to viruses. In Ogra PL, Mestecky J, Lamm M, Strober W, McGhee J, Bienenstock J, eds. *Mucosal Immunology: Vol. I. Cellular Basis of Mucosal Immunity*. Academic Press, Inc. 1994;333-343.
279. Subbarao EK, Kawaoka Y, **Murphy BR**. A new strategy for the development of a genetically engineered live, attenuated influenza A virus vaccine. In Brown F, Chanock RM, Ginsberg HS, Norrby E, eds. *Vaccines 94: Modern Approaches to New Vaccines Including Prevention of AIDS*. Cold Spring Harbor: Cold Spring Harbor Laboratory Press 1994;373-380.
280. Treanor J, Perkins M, Battaglia R, **Murphy BR**. Evaluation of the genetic stability of the temperature-sensitive PB2 gene mutation of the influenza A/Ann Arbor/6/60 cold-adapted vaccine virus. *J Virol* 1994;68:7684-7688.
281. Collins PL, Hill MG, Camargo E, Grosfeld H, Chanock RM, **Murphy BR**. Production of infectious human respiratory syncytial virus from cloned cDNA confirms an essential role for the transcription elongation factor from the 5' proximal open reading frame of the M2 mRNA in gene expression and provides a capability for vaccine development. *Proc Natl Acad Sci USA* 1995;92:11563-11567.
282. Connors M, Crowe JE Jr, Firestone C-Y, **Murphy BR**, Collins PL. A cold-passaged, attenuated strain of human respiratory syncytial virus contains mutations in the F and L genes. *Virology* 1995;208:478-484.
283. Crowe JE Jr, Bui PT, Siber GR, Elkins WR, Chanock RM, **Murphy BR**. Cold-passaged, temperature sensitive mutants of human respiratory syncytial virus (RSV) are highly attenuated, immunogenic, and protective in seronegative chimpanzees, even when RSV antibodies are infused shortly before immunization. *Vaccine* 1995;13:847-855.
284. Crowe JE Jr, Cheung PYK, Wallace EF, Chanock RM, Lerrick JW, **Murphy BR**, Fry K. Isolation and characterization of a chimpanzee monoclonal antibody to the G-glycoprotein of human respiratory syncytial virus. *Clin Diag Lab Immun* 1995;1:701-706.
285. Crowe JE Jr, Wright P, Clements ML, Karron R, Collins P, Chanock R, Murphy B. Live attenuated respiratory syncytial virus vaccine candidates that are satisfactorily attenuated

and genetically stable. In *Vaccines, One Hundred Years After Louis Pasteur*, The Year of Louis Pasteur International Symposia. Paris, France: Institut Pasteur 1995;211-214.

286. Epstein SL, Lo C-Y, Misplon JA, **Murphy BR**, Lawson CM, Subbarao EK. Mediators of heterosubtypic immunity to influenza A virus infection in mice. In Chanock RM, Brown F, Ginsberg HS, Norrby E, eds. *Vaccines 95: Modern Approaches to New Vaccines Including Prevention of AIDS*. Cold Spring Harbor: Cold Spring Harbor Laboratory Press 1995;393-397.
287. Hsu K-HL, Crowe JE Jr, Lubeck MD, Davis AR, Hung PP, Chanock RM, **Murphy BR**. Isolation and characterization of a highly attenuated respiratory syncytial virus (RSV) vaccine candidate by mutagenesis of the incompletely attenuated RSV A2 ts-1 NG-1 mutant virus. *Vaccine* 1995;13:509-515.
288. Karron RA, Subbarao EK, Wilson MH, The Pediatric Care Center, Clements ML, **Murphy BR**. Safety and immunogenicity of a cold-adapted influenza A (H1N1) reassortant virus vaccine administered to infants less than six months of age. *Pediatr Infect Dis J* 1995;14:10-16.
289. Karron RA, Wright PF, Hall SL, Makhene M, Thompson J, Burns BA, Tollefson S, Steinhoff MC, Wilson MH, Harris DO, Clements ML, **Murphy BR**. Safety and immunogenicity of a bovine parainfluenza 3 virus vaccine in infants and young children. *J Infect Dis* 1995;171:1107-1114.
290. Karron RA, Wright PF, Newman FK, Makhene M, Thompson J, Samorodin R, Wilson MH, Anderson EL, Clements ML, **Murphy BR**, Belshe RB. A live human parainfluenza type 3 virus vaccine is attenuated and immunogenic in healthy infants and children. *J Infect Dis* 1995;172:1445-1450.
291. Kulkarni AB, Collins PL, Bacik I, Yewdell JW, Bennink JR, Crowe JE Jr., **Murphy BR**. Cytotoxic T-cells specific for a single peptide on the M2 protein of respiratory syncytial virus are the sole mediators of resistance induced by immunization with M2 encoded by a recombinant vaccinia virus. *J Virol* 1995;69:1261-1264.
292. Moldoveanu Z, Clements ML, Prince SJ, **Murphy BR**, Mestecky J. Human immune responses to influenza virus vaccines administered by systemic or mucosal routes. *Vaccine* 1995;13:1006-1012.
293. **Murphy BR**, Crowe JE Jr, Lubeck MD, Hsu K-HL, Hall SL, Karron RA, Clements ML, Wright PF, Belshe RB, Chanock RM. Live attenuated vaccines for respiratory syncytial virus and parainfluenza virus type 3. In *Strategies for Pediatric Vaccines: Conventional and Molecular Approaches*. The Report of the 104th Ross Conference on Pediatric Research. Columbus, OH: Ross Products Division, Abbott Laboratories 1995;173-178.
294. **Murphy BR**, Karron R, Wright P, Belshe R, Clements ML. Two live attenuated parainfluenza virus type 3 (PIV3) candidate vaccines are safe, genetically stable, and immunogenic in seronegative infants and young children. In *Vaccines, One Hundred Years After Louis Pasteur*, The Year of Louis Pasteur International Symposia. Paris, France: Institut Pasteur 1995;209-210.

295. Subbarao K, Webster RG, Kawaoka Y, **Murphy BR**. Are there alternative avian influenza viruses for generation of stable attenuated avian-human influenza A reassortant viruses? *Virus Res* 1995;39:105-118.
296. Subbarao EK, Park EJ, Lawson CM, Chen AF, **Murphy BR**. Sequential addition of temperature-sensitive missense mutations into the PB2 gene of influenza A transfected viruses can effect an increase in temperature sensitivity and attenuation and permits the rational design of a genetically engineered live influenza A virus vaccine. *J Virol* 1995;69:5969-5977.
297. Clements ML, Makhene MK, Karron RA, **Murphy BR**, Steinhoff MC, Subbarao K, Wilson MH, The Pediatric Care Center, Wright PF. Effective immunization with live attenuated influenza A virus can be achieved in early infancy. *J Infect Dis* 1996;173:44-51.
298. Crowe JE Jr, Bui PT, Firestone C-Y, Connors M, Elkins WR, Chanock RM, **Murphy BR**. Live subgroup B respiratory syncytial virus (RSV) vaccines that are attenuated, genetically stable, and immunogenic in rodents and nonhuman primates. *J Infect Dis* 1996;173:829-839.
299. Crowe JE Jr, Firestone C-Y, Whitehead SS, Collins PL, **Murphy BR**. Acquisition of the *ts* phenotype by a chemically mutagenized cold-passaged human respiratory syncytial virus vaccine candidate results from the acquisition of a single mutation in the polymerase (L) gene. *Virus Genes* 1996;13:269-273.
300. Firestone C-Y, Whitehead SS, Collins PL, **Murphy BR**, Crowe, JE. Nucleotide sequence analysis of the respiratory syncytial virus (RSV) subgroup A cold-passaged (*cp*) temperature sensitive (*ts*) cpts-248/404 live attenuated virus vaccine candidate. *Virology* 1996;225:419-422.
301. Jin H, Subbarao K, Bagai S, Leser GP, **Murphy BR**, Lamb RA. Palmitylation of the influenza virus hemagglutinin is not essential for virus assembly or infectivity. *J Virol* 1996;70:1406-1414.
302. Karron RA, Makhene M, Gay K, Wilson MH, Clements ML, **Murphy BR**. Evaluation of a live attenuated bovine parainfluenza type 3 vaccine in 2 to 6 month old infants. *Pediat Infect Dis* 1996;15:650-654.
303. **Murphy BR**, Chanock RM. Immunization against virus disease. In Fields BN, Knipe D, Howley P, Chanock RM, Melnick JL, Monath TP, Roizman B, Straus SE, eds. *Fields Virology* (Third Edition). New York, NY: Raven Press 1996;467-497.
304. **Murphy BR**, Webster RG. Orthomyxoviruses. In Fields BN, Knipe D, Howley P, Chanock RM, Melnick JL, Monath TP, Roizman B, Straus SE, eds. *Fields Virology* (Third Edition). New York, NY: Raven Press 1996;1397-1445.
305. Subbarao K, Cianci C, Krystal M, **Murphy BR**. Identification of an amino acid associated with the endonuclease function of the PB2 protein of an influenza A virus. In

*Options for the control of influenza III*, Excerpta Medica International Congress Series, Elsevier Science 1996;427-432.

306. Subbarao K, Park EJ, Gottlieb P, **Murphy BR**. Use of viruses bearing a PB2 gene containing three introduced temperature-sensitive mutations as live, attenuated influenza A virus vaccines. *Options for the control of influenza III*, Excerpta Medica International Congress Series, Elsevier Science 1996;782-787.
307. Wyatt LS, Shors ST, **Murphy BR**, Moss B. Development of a replication-deficient recombinant vaccinia virus vaccine effective against parainfluenza virus 3 infection in an animal model. *Vaccine* 1996;14(15):1451-1458.
308. Bukreyev A, Whitehead SS, **Murphy BR**, Collins PL. Recombinant respiratory syncytial virus from which the entire SH gene has been deleted grows efficiently in cell culture and exhibits site-specific attenuation in the respiratory tract of the mouse. *J Virol* 1997;12:8973-8982.
309. Crowe JE Jr, Collins PL, Chanock RM, **Murphy BR**. Vaccines against respiratory syncytial virus (RSV) and parainfluenza virus type 3 (PIV3). In Levine MM, Woodrow GC, Kaper JB, Cobon, GS, eds. *New Generation Vaccine*; Marcel Dekker, Inc New York, NY 1997;711-725.
310. Durbin AP, Hall SL, Siew JW, Whitehead SS, Collins PL, **Murphy BR**. Recovery of infectious human parainfluenza virus type 3 from cDNA. *Virology* 1997;235:323-332.
311. Durbin AP, Siew JW, **Murphy BR**, Collins PL. Minimum protein requirements for transcription and RNA replication of a minigenome of human parainfluenza virus type 3 and evaluation of the rule of six. *Virology* 1997;234:74-83.
312. Juhasz K, Whitehead SS, Bui PT, Biggs JM, Boulanger CA, Collins PL, **Murphy BR**. The temperature-sensitive (ts) phenotype of a cold-passaged (cp) live attenuated respiratory syncytial virus vaccine candidate, designated cpts530, results from a single amino acid substitution in the L protein. *J Virol* 1997;71:5814-5819.
313. Karron RA, Buonagurio DA, Georgiu AF, Whitehead SS, Adamus JE, Clements-Mann ML, Harris DO, Randolph VB, Udem SA, **Murphy BR**, Sidhu MS. Respiratory Syncytial Virus (RSV) SH and G proteins are not essential for viral replication *in vitro*: clinical evaluation and molecular characterization of a cold-passaged, attenuated RSV subgroup B mutant. *Proc Natl Acad Sci USA* 1997;94:13961-13966.
314. Karron RA, Wright PF, Crowe JE Jr, Clements ML, Thompson J, Makhene M, Casey R, **Murphy BR**. Evaluation of two live, cold-passaged, temperature-sensitive respiratory syncytial virus (RSV) vaccines in chimpanzees, adults, infants and children. *J Infect Dis* 1997;176:1428-1436.
315. **Murphy BR**, Collins PL. Current status of respiratory syncytial virus (RSV) and parainfluenza virus type 3 (PIV3) vaccine development: *Memorandum from a Joint WHO/NIAID meeting* 1997; *Bull WHO* 75:307-313.

316. Murphy BR, Park EJ, Gottlieb P, Subbarao K. An influenza A live attenuated reassortant virus possessing three temperature-sensitive mutations in the PB2 polymerase gene rapidly loses temperature sensitivity following replication in hamsters. *Vaccine* 1997;15:1372-1378.
317. Crowe JE Jr, Firestone C-Y, Beeler JA, Coelingh KL, Burton DR, Chanock RM, Murphy BR. Monoclonal antibody-resistant mutants selected with a respiratory syncytial virus (RSV) neutralizing human antibody fab fragment (Fab19) define a unique epitope on the fusion (F) glycoprotein. *Virology* 1998;252:373-375.
318. Crowe JE Jr, Gilmour PS, Murphy BR, Chanock RM, Lingxun D, Pomerantz RJ, Pilkington GR. Isolation of a second recombinant human respiratory syncytial virus (RSV) monoclonal antibody fragment (Fab RSVF2-5) that exhibits therapeutic efficacy in vivo. *J Infect Dis* 1998;177:1073-1076.
319. Durbin AP, Wyatt LS, Siew J, Moss B, Murphy BR. The immunogenicity and efficacy of intranasally or parenterally administered replication-deficient vaccinia-parainfluenza virus type 3 recombinants in rhesus monkeys. *Vaccine* 1998;16:1324-1330.
320. Murphy BR. Parainfluenza viruses. In Gorbach SL, Bartlett JG, Blacklow NR, eds. *Infectious Diseases, Second Edition*. Philadelphia, PA: W.B. Saunders Company 1998;2125-2130.
321. Skiadopoulos MH, Durbin AP, Tatem JM, Wu S-L, Paschalis M, Tao T, Collins PL, Murphy BR. Three amino acid substitutions in the L protein of the human parainfluenza virus type 3 cp45 live attenuated vaccine candidate contribute to its temperature-sensitive and attenuation phenotypes. *J Virol* 1998;72:1762-1768.
322. Tao T, Durbin AP, Whitehead SS, Davoodi F, Collins PL, Murphy BR. Recovery of a fully viable chimeric human parainfluenza virus (PIV) type 3 in which the hemagglutinin-neuraminidase and fusion glycoproteins have been replaced by those of PIV type 1. *J Virol* 1998;72:2955-2961.
323. Whitehead SS, Firestone C-Y, Collins PL, Murphy BR. A single nucleotide substitution in the transcription start signal of the M2 gene of respiratory syncytial virus vaccine candidate cpts248/404 is the major determinant of the temperature-sensitive and attenuation phenotypes. *Virology* 1998;247:232-239.
324. Whitehead SS, Juhasz K, Firestone C-Y, Collins PL, Murphy BR. Recombinant respiratory syncytial virus (RSV) bearing a set of mutations from cold-passaged RSV is attenuated in chimpanzees. *J Virol* 1998;72:4467-4471.
325. Auwaerter PG, Rota PA, Elkins WR, Adams RJ, DeLozier T, Shi Y, Bellini WJ, Murphy BR, Griffin DE. Measles virus infection in rhesus macaques: Altered immune responses and comparison of the virulence of six different virus strains. *J Infect Dis* 1999;180:950-958.
326. Bukreyev A, Whitehead SS, Bukreyeva N, Murphy BR, Collins PL. Interferon gamma expressed by a recombinant respiratory syncytial virus attenuates virus replication in

mice without compromising immunogenicity. *Proc Natl Acad Sc USA* 1999;96:2367-2372.

327. Collins PL, Whitehead SS, Bukreyev A, Fearn R, Teng MN, Juhasz K, Chanock RM, **Murphy BR**. Rational design of a live-attenuated recombinant vaccine virus for human respiratory syncytial virus by reverse genetics. *Adv Virus Res* 1999;54:423-451.

328. Crowe Jr. JE, Randolph V, **Murphy BR**. The live attenuated subgroup B respiratory syncytial virus (RSV) vaccine candidate RSV 2B33F is attenuated and immunogenic in chimpanzees, but exhibits partial loss of the *ts* phenotype following replication *in vivo*. *Virus Res* 1999;59:13-22.

329. Durbin AP, Cho CJ, Elkins WR, Wyatt LS, Moss B, **Murphy BR**. Comparison of the immunogenicity and efficacy of a replication-defective vaccinia virus expressing antigens of human parainfluenza virus type 3 (HPIV3) with that of a live attenuated HPIV3 vaccine candidate in rhesus monkeys passively immunized with PIV3 antibodies. *J Infect Dis* 1999;179:1345-1351.

330. Durbin AP, McAuliffe JM, Collins PL, **Murphy BR**. Mutations in the C, D, and V open reading frames of human parainfluenza virus type 3 attenuate replication in rodents and primates. *Virology* 1999;261:319-330.

331. Juhasz K, **Murphy BR**, Collins PL. The major attenuating mutations of the respiratory syncytial virus vaccine candidate cpts530/1009 specify temperature-sensitive defects in transcription and replication and a non-temperature sensitive alteration in mRNA termination. *J Virol* 1999;73:5176-5180.

332. Juhasz K, Whitehead SS, Boulanger CA, Firestone C-Y, Collins PL, **Murphy BR**. The two amino acid substitutions in the L protein of cpts530/1009, a live-attenuated respiratory syncytial virus candidate vaccine, are independent temperature-sensitive and attenuation mutations. *Vaccine* 1999;17:1416-1424.

333. **Murphy BR**. Mucosal Immunity to Viruses. In Ogra P, Mestecky J, Lamm M, Strober W, McGhee J, Bienenstock J, eds., *Mucosal Immunology 2nd ed.*, San Diego, CA. Academic Press 1999;695-708.

334. Skiadopoulos MH, Surman S, Tatem JM, Paschal M, Wu SL, Udem SA, Durbin AP, Collins PL, **Murphy BR**. Identification of mutations contributing to the temperature-sensitive, cold-adapted, and attenuation phenotypes of the live attenuated cold-passage 45 (*cp45*) human parainfluenza virus 3 candidate vaccine. *J Virol* 1999;73:1374-1381.

335. Skiadopoulos MH, Surman SR, St. Claire M, Elkins WR, Collins PL, **Murphy BR**. Attenuation of the recombinant human parainfluenza virus type 3 *cp45* candidate vaccine virus is augmented by importation of the respiratory syncytial virus *cpts530* L polymerase mutation. *Virology* 1999;260:125-135.

336. Skiadopoulos MH, Tao T, Surman SR, Collins PL, **Murphy BR**. Generation of a parainfluenza virus type 1 vaccine candidate by replacing the HN and F glycoproteins of

the live-attenuated PIV3 *cp45* vaccine virus with their PIV1 counterparts. *Vaccine* 1999;18:503-510.

337. Tao T, Skiadopoulos MH, Durbin AP, Davoodi F, Collins PL, **Murphy BR**. A live attenuated chimeric recombinant parainfluenza virus (PIV) encoding the internal proteins of PIV type 3 and the surface glycoproteins of PIV type 1 induces complete resistance to PIV1 challenge and partial resistance to PIV3 challenge. *Vaccine* 1999;17:1100-1108.

338. Whitehead SS, Bukreyev A, Teng MN, Firestone CY, St. Clair M, Elkins WR, Collins PL, **Murphy BR**. Recombinant respiratory syncytial virus (RSV) bearing a deletion of either the NS2 or SH gene is attenuated in chimpanzees. *J Virol* 1999;73:3438-3442.

339. Whitehead SS, Firestone CY, Karron RA, Crowe JE, Jr., Elkins WR, Collins PL, **Murphy BR**. Addition of a missense mutation present in the L gene of respiratory syncytial virus (RSV) *cpts* 530/1030 to RSV vaccine candidate *cpts* 248/404 increases its attenuation and temperature sensitivity. *J Virol* 1999;73:871-877.

340. Whitehead SS, Hill MG, Firestone CY, St. Claire M, Elkins WR, **Murphy BR**, Collins PL. Replacement of the F and G protective surface antigens of respiratory syncytial virus subgroup A with those of subgroup B generates chimeric live attenuated RSV subgroup B vaccine candidates. *J Virol* 1999;73:9773-9780.

341. Wyatt LS, Whitehead SS, Venanzi KA, **Murphy BR**, Moss B. Priming and boosting immunity to respiratory syncytial virus by recombinant replication-defective vaccinia virus MVA. *Vaccine* 1999;18:392-397.

342. Bailly JE, McAuliffe JM, Durbin AP, Elkins WR, Collins PL, **Murphy BR**. A recombinant human parainfluenza virus type 3 (PIV3) in which the nucleocapsid N protein has been replaced by that of bovine PIV3 is attenuated in primates. *J Virol* 2000;74:3188-3195.

343. Bailly JE, McAuliffe JM, Skiadopoulos MH, Collins PL, **Murphy BR**. Sequence determination and molecular analysis of two strains of bovine parainfluenza virus type 3 that are attenuated for primates. *Virus Genes* 2000;20:173-182.

344. Buchholz UJ, Granzow H, Schuldt K, Whitehead SS, **Murphy BR**, Collins PL. Chimeric bovine respiratory syncytial virus with glycoprotein gene substitutions from human respiratory syncytial virus (HRSV): effects on host range and evaluation as a live-attenuated HRSV vaccine. *J. Virol* 2000;74:1187-1199.

345. Bukreyev A, **Murphy BR**, Collins PL. Respiratory syncytial virus can tolerate an intergenic sequence of at least 160 nucleotides with little effect on transcription or replication in vitro and in vivo. *J Virol* 2000;74:11017-11026.

346. Bukreyev A, Whitehead SS, Prussin C, **Murphy BR**, Collins PL. Effect of co-expression of IL-2 by recombinant respiratory syncytial virus on virus replication, immunogenicity and production of other cytokines. *J Virol* 2000;74:7151-7157.

347. Durbin AP, Elkins WR, **Murphy BR**. African green monkeys provide a useful nonhuman primate model for the study of human parainfluenza virus types -1, -2, and -3 infection. *Vaccine* 2000;18:2462-2469.

348. Durbin AP, Skiadopoulos MH, McAuliffe JM, Riggs JM, Surman SR, Collins PL, **Murphy BR**. Human parainfluenza type 3 (PIV3) expressing the hemagglutinin protein of measles virus provides a potential method for immunization against measles virus and PIV3 in early infancy. *J Virol* 2000;74:6821-6831.

349. Feller JA, Smallwood S, Skiadopoulos MH, **Murphy BR**, Moyer SA. Comparison of identical temperature sensitive mutations in the L polymerase proteins of Sendai, parainfluenza 3 and vesicular stomatitis viruses. *Virology* 2000;276:190-201.

350. Gonzalez IM, Karron RA, Eichelberger M, Walsh EE, Delagarza VW, Bennett R, Chanock RM, **Murphy BR**, Clements-Mann ML, Falsey AR. Evaluation of the live attenuated *cpts* 248/404 RSV vaccine in combination with a subunit RSV vaccine (PFP-2) in healthy young and older adults. *Vaccine*, 2000;18:1763-1772.

351. Munoz FM, Galasso GJ, Gwaltney J, Hayden FG, **Murphy B**, Webster R, Wright P, Couch RB. Current research on influenza and other respiratory viruses: II International Symposium. *Anitviral Res* 2000;46(2):91-124.

352. Schmidt AC, McAuliffe JM, Huang A, Surman SR, Bailly JE, Elkins WR, Collins PL, **Murphy BR**, Skiadopoulos MH. Bovine parainfluenza virus type 3 fusion and hemagglutinin-neuraminidase glycoproteins make an important contribution to the restricted replication of BPIV3 in primates. *J Virol* 2000;74:8922-8929.

353. Skiadopoulos MH, Surman SR, Durbin AP, Collins PL, **Murphy BR**. Long nucleotide insertions between the HN and L protein coding regions of human parainfluenza virus type 3 yield viruses with temperature sensitive and host-range attenuation phenotypes. *Virology* 2000;272:225-234.

354. Tao T, Davoodi F, Cho CJ, Skiadopoulos MH, Durbin AP, Collins PL, **Murphy BR**. A live attenuated recombinant chimeric parainfluenza virus (PIV) candidate vaccine containing the hemagglutinin-neuraminidase and fusion glycoproteins of PIV1 and the remaining proteins from PIV3 induces resistance to PIV1 even in animals immune to PIV3. *Vaccine* 2000;18:1359-1366.

355. Tao T, Skiadopoulos MH, Davoodi F, Riggs JM, Collins PL, **Murphy BR**. Replacement of the ectodomains of the hemagglutinin-neuraminidase and fusion glycoproteins of recombinant parainfluenza virus type 3 (PIV3) with their counterparts from PIV2 yields attenuated PIV2 vaccine candidates. *J Virol* 2000;74(14):6448-6458.

356. Teng MN, Whitehead SS, Birmingham A, St. Claire M, Elkins WR, **Murphy BR**, Collins PL. Recombinant respiratory syncytial virus that does not express NS1 or M2-2 protein is highly attenuated and immunogenic in chimpanzees. *J Virol* 2000;74(19):9317-9321.

357. Wright PF, Karron RA, Belshe RB, Thompson J, Crowe JE, Jr., Boyce TG, Halburnt LL, Reed GW, Whitehead SS, Anderson EL, Wittek AE, Casey R, Eichelberger M, Thumar B, Randolph VB, Udem SA, Chanock RM, **Murphy BR**. Evaluation of a cold-passaged, temperature-sensitive, respiratory syncytial virus (RSV) vaccine candidate in infancy. *J Infect Dis* 2000;182(5):1331-1342.

358. Blaney JE, Jr., Johnson DH, Firestone C-Y, Hanson CT, **Murphy BR**, Whitehead SS. Chemical mutagenesis of dengue virus type 4 yields mutant viruses which are temperature-sensitive in Vero cells or human liver cells and attenuated in mice. *J Virol* 2001;75:9731-9740.

359. Bukreyev A, Belyakov IM, Berzofsky JA, **Murphy BR**, Collins PL. Granulocyte-macrophage colony-stimulating factor expressed by recombinant respiratory syncytial virus attenuates viral replication and increases the level of pulmonary antigen presenting cells. *J Virol* 2001;75:12128-12140.

360. Chanock RM, **Murphy BR**, Collins PL. Parainfluenza Viruses. In Knipe DM, Howley PM, eds. *Fields Virology*. New York, NY: Raven Press 2001;1341-1380.

361. Collins PL, Chanock RM, **Murphy BR**. Respiratory Syncytial Virus. In Knipe DM, Howley PM, eds. *Fields Virology*. New York, NY: Raven Press 2001;1443-1486.

362. Crowe JE, Jr., Firestone C-Y, **Murphy BR**. Passively-acquired antibodies suppress humoral but not cell-mediated immunity in mice immunized with live attenuated respiratory syncytial virus vaccines. *J Immunology* 2001;167:3910-18.

363. Durbin AP, Karron RA, Sun W, Vaughn DW, Reynolds MJ, Perreault JR, Thumar B, Men R, Lai CJ, Elkins WR, Chanock RM, **Murphy BR**, Whitehead SS. Attenuation and immunogenicity in humans of a live dengue virus type-4 vaccine candidate with a 30 nucleotide deletion in its 3'-untranslated region. *Am J Trop Med Hyg* 2001;65(5):405-13.

364. Harro CD, Pang YY, Roden RB, Hildesheim A, Wang Z, Reynolds JM, Mast TC, Robinson R, **Murphy BR**, Karron RA, Dillner J, Schiller JT, Lowy DR. Safety and immunogenicity trial in adult volunteers of a human papillomavirus 16 L1 virus-like particle vaccine. *J Natl Cancer Inst* 2001;93:284-292.

365. **Murphy BR**, Chanock RM. Immunization against viral diseases. In Knipe DM, Howley PM, eds. *Fields Virology*. New York, NY: Raven Press 2001;435-468.

366. Schmidt AC, McAuliffe JM, **Murphy BR**, Collins PL. Recombinant bovine/human parainfluenza virus type 3 (B/HPIV3) expressing the respiratory syncytial virus (RSV) G and F proteins can be used to achieve simultaneous mucosal immunization against RSV and HPIV3. *J Virol* 2001;75:4594-4603.

367. Schmidt AC, Couch RB, Galasso GJ, Hayden FG, Mills J, **Murphy BR**, Chanock RM. Current research on respiratory viral infections: Third International Symposium. *Antiviral Res* 2001;50:157-196.

368. Skiadopoulos MH, Surman SR, Riggs JM, Collins PL, **Murphy BR**. A chimeric human-bovine parainfluenza virus type 3 expressing measles virus hemagglutinin protein is attenuated for replication but is still immunogenic in rhesus monkeys. *J Virol* 2001;75:10498-10504.

369. Tao T, Skiadopoulos MH, Davoodi F, Surman SR, Collins PL, **Murphy BR**. Construction of a live-attenuated bivalent vaccine virus against human parainfluenza virus (PIV) types 1 and 2 using a recombinant PIV3 backbone. *Vaccine* 2001;19:3620-3631.

370. Troyer JM, Hanley KA, Whitehead SS, Strickman D, Karron RA, Durbin AP, **Murphy BR**. A live attenuated dengue-4 virus vaccine candidate with a 30 base pair deletion in its 3' untranslated region has restricted capacity for dissemination in mosquitoes and is not transmitted from vaccinees to mosquitoes. *Am J Trop Med Hyg* 2001;65:414-19.

371. Collins PL, Chanock RM, **Murphy BR**. Respiratory syncytial virus: reverse genetics and vaccine strategies. *Virology* 2002;296:204-211.

372. Hanley KA, Lee JJ, Blaney JE, Jr., **Murphy BR**, Whitehead SS. Paired charge-to-alanine mutagenesis of dengue virus type 4 NS5 generates mutants with temperature-sensitive, host-range and mouse-attenuation phenotypes. *J Virol* 2002;76:525-31.

373. **Murphy BR**, Coelingh K. Principles underlying the development and use of live attenuated cold-adapted influenza A and B virus vaccines. Review. *Viral Immunology* 2002;15(2):295-323.

374. **Murphy BR**, Collins PL. Live-attenuated virus vaccines for respiratory syncytial and parainfluenza viruses: applications of reverse genetics. *J Clin Investig* 2002;110(1):21-27.

375. Newman JT, Surman SR, Riggs JM, Hanson CT, Collins PL, **Murphy BR**, Skiadopoulos MH. Sequence analysis of the Washington/1964 strain of human parainfluenza virus type 1 (HPIV1) and recovery and characterization of wild type recombinant HPIV1 produced by reverse genetics. *Virus Genes* 2002;24:77-92.

376. Schmidt AC, Wenzke D, McAuliffe JM, Elkins WR, **Murphy BR**, Collins PL. Mucosal immunization of rhesus monkeys against RSV subgroup A, subgroup B and HPIV3 using cDNA-derived bovine/human parainfluenza virus type 3 (B/HPIV3) expressing the respiratory syncytial virus (RSV) G and F proteins. *J Virol* 2002;76:1089-99.

377. Skiadopoulos MH, Surman SR, Riggs JM, Elkins WR, St. Claire M, Kolakofsky D, Collins PL, **Murphy BR**. Sendai virus, a murine parainfluenza virus type 1, replicates to a level similar to human PIV1 in the upper and lower respiratory tract of African green monkeys and chimpanzees. *Virology* 2002;297:153-160.

378. Skiadopoulos MH, Surman SR, Riggs JM, Örvell C, Collins PL, **Murphy BR**. Evaluation of the replication and immunogenicity of recombinant human parainfluenza virus type 3 vectors expressing up to three foreign glycoproteins. *Virology* 2002;297:136-152.

379. Skiadopoulos MH, Tatem JM, Surman SR, Mitcho Y, Wu S-L, Elkins R, **Murphy BR**. The recombinant chimeric human parainfluenza virus type 1 vaccine candidate, rHPIV3-1cp45, is attenuated, immunogenic and protective in African green monkeys. *Vaccine* 2002;20:1846-52.

**SUBMITTED OR IN PRESS**

Blaney JE, Jr., Johnson DH, Firestone C-Y, Hanson CT, **Murphy BR**, Whitehead SS. Temperature-sensitive mutants of dengue virus type 4 with specific defects in replication in Vero cells or human liver cells are attenuated in mice. *Virology* 2001, accepted.

Blaney JE, Jr., Manipon GG, **Murphy BR**, Whitehead SS. Temperature sensitive mutations in the genes encoding the NS1, NS2A, NS3, and NS5 nonstructural proteins of dengue virus type 4 restrict replication in the brains of mice. *J Virol* 2002, submitted.

Bukreyev A, Skiadopoulos MH, McAuliffe J, **Murphy BR**, Collins PL, Schmidt AC. More antibody with less antigen: can immunogenicity of attenuated live virus vaccines be improved? *Proc Natl Acad Sci USA* 2002, submitted.

Cortez K, **Murphy BR**, Almeida KN, Beeler J, Levandowski RA, Gill VJ, Childs RW, Barrett AJ, Smolskis M, Bennett JE. Immune globulin prophylaxis of respiratory syncytial virus infection in stem cell transplant recipients. *J Infect Dis* 2002, in press.

Crowe JE, Collins PL, **Murphy BR**. Vaccines against respiratory syncytial virus (RSV) and parainfluenza virus types 1-3 (PIV1-3). In *New Generation Vaccines*. 2002.

Krempl C, **Murphy BR**, Collins PL. Recombinant respiratory syncytial virus with the G and F genes shifted to the promoter-proximal positions. *J Virol* 2002, accepted.

Skiadopoulos MH, Schmidt AC, Riggs JM, Surman SR, Elkins WR, St. Claire M, Collins PL, **Murphy BR**. The determinants of the host-range restriction of replication of bovine parainfluenza virus type 3 (BPIV3) in rhesus monkeys are polygenic. *J Virol* 2002, submitted.

Skiadopoulos MH, Vogel L, Riggs JM, Surman SR, Collins PL, **Murphy BR**. The genome length of human parainfluenza virus type 2 (HPIV2) follows the rule of six, and recombinant viruses recovered from non-polyhexameric length antigenomic cDNAs contain a biased distribution of correcting mutations. *J Virol*, 2002, submitted.

Whitehead SS, Falgout B, Hanley KA, Blaney JE, Jr., Markoff L, **Murphy BR**. A live attenuated dengue virus type 1 vaccine candidate with a 30 nucleotide deletion in the 3' untranslated region is highly attenuated and immunogenic in monkeys. *J Virol* 2002, submitted.